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The American Heart Journal

VOL. 15 JUNE, 1938 NO. 6

Original Communications

CLINICAL STUDIES OF GITALIN AND OF DIGITALIS IN THE TREATMENT OF AURICULAR FIBRILLATION*

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THE present study was undertaken to compare clinically the actions of digitalis leaf and gitalin.† In 1912 Kraft[1] obtained a new substance from a cold water extract of digitalis leaves. The drug which he called gitalin was subsequently introduced under the name of verodigen. Gitalin (amorphous) is a glucosidal fraction of *Digitalis purpurea* which is extracted from a cold water infusion by means of chloroform after the removal of saponins and digitalic acids with basic lead acetate. The chloroform extract is concentrated *in vacuo* and the amorphous gitalin precipitated with petroleum ether, and subsequently dried without heat to constant weight. It occurs as a yellowish-white amorphous powder which is very soluble in chloroform and alcohol, and in about 800 parts of cold water. In the dry state gitalin (amorphous) is stable, as shown by biologic assays over periods of years. The potency is apparently quite uniform and the minimum lethal dose by the Hatcher-Brody cat method[2] is approximately 0.8 mg. per kilogram.[3] Straub[4] found from his pharmocologic studies that gitalin possesses all the properties common to the digitalis bodies. The more important European communications dealing with the actions of gitalin are reviewed by Mansfeld and Horn.[5] The clinical potency of gitalin and of other digitalis bodies does not always correspond to the biologically determined potency; hence reports in the literature are conflicting. The European studies (both pharmocologic and clinical) indicate that 0.8 mg. (1/80 grain) of gitalin is equivalent to 0.1 gram of digitalis leaf.[4, 5] Stroud found that the quantity of gitalin representing one cat unit biologically (0.8 mg.) did the work clinically of 3 cat units (0.3 gm.) of digitalis. Our own studies show that the biological cat unit of gitalin (0.8 mg.) is equivalent clinically

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†The drugs used in this study were supplied by the Rare Chemical Company, Nepera Park, New York.

to 2 cat units of digitalis (0.2 gm.). In a recent study[6] of urginin, a squill glucoside, a discrepancy between clinical and biologic units of the drug was also found; approximately 2 cat units of urginin were required to obtain the same clinical effects as 1 cat unit of digitalis.

MATERIAL

Thirty-six ambulant patients with auricular fibrillation were observed at our office for periods of six to thirteen months. Each patient was seen from fifteen to twenty times during the study. There were twenty-one women, the majority of whom were housewives, and fifteen men, nearly all of whom were workers at occupations calling for slight to moderate exertion. Twenty-eight patients (78 per cent) had chronic rheumatic valvular disease; one (3 per cent) had had a coronary thrombosis; and one (3 per cent) had hyperthyroidism. The remaining six patients (16 per cent), all men, had no evidence of valvular disease, coronary arteriosclerosis, hyperthyroidism, or previous hypertension. The cause of their cardiac irregularity is unknown. For the entire group, the average age at the onset of auricular fibrillation was 41.6 years. Auricular fibrillation had existed, on the average, for 2.6 years prior to the beginning of the study. This figure was greatly lowered by the fact that several patients presented themselves for the first time at the onset of their irregularity. There were eight patients in whom auricular fibrillation had lasted four or more years; one, seven years; and one, nine years. The longest period of auricular fibrillation occurred in a man aged 64 years, in whom it had commenced twenty-one years previously, at the age of 43 years. In him the auricular fibrillation is of unknown etiology.

At the time of the study, the average age of the patients was 44.2 years. In twenty-eight of the thirty-six patients the blood pressure was normal; in eight there was some degree of hypertension, ranging from 150 systolic to a maximum of 190 systolic. The left auricle was enlarged in all cases except one, as determined by fluoroscopy; the enlargement was moderate in nine cases, marked in nineteen cases, and extreme in seven cases.

During the study there was only one death. Progressive dyspnea, cough, frank hemoptysis, irregular fever, basal pulmonary signs, and increasing scleral icterus suggested that reactivation of the rheumatic process was the immediate cause of this patient's progressive heart failure and death. It is of some interest that he was the only patient whose subjective symptoms, including his cough, which was at times productive of blood, were out of proportion to his physical findings. These symptoms, very likely due to reinfection, were present for months before the more acute terminal illness. The rôle of reinfection in persons dying with rheumatic heart disease has been stressed in recent years.[7]

In twenty-seven patients the maintenance doses of both gitalin and of digitalis were established. By "maintenance dose," we mean the smallest amount which would keep the patient comfortable and maintain his ventricular rate at approximately 68 to 88 beats per minute. Each drug was administered long enough to be sure that the minimal dose was constant. Due consideration was given to the discrepancy between the maximum and the minimum digitalis dosage necessary for clinical maintenance.[8] The heart rates were counted either by stethoscope or from electrocardiographic tracings after the patients had been resting on the examining table for at least one minute, and after a preliminary rest period in the waiting room for at least ten minutes. Gitalin was given first in each case. It was dispensed in tablets of 1/80 grain, scored into three equal parts. After the maintenance dose had been ascertained, which usually required several weeks, the gitalin

was replaced by a standard preparation of digitalis (dried leaves, each tablet containing 1½ grains, i.e., 1 cat unit). The dose of digitalis was then adjusted over a period of several weeks until approximately the same heart rate was obtained.

RESULTS

The results are summarized in Table I, which shows that the daily maintenance dose of digitalis was ½ cat unit in two patients, 1 cat unit in ten patients, 1½ cat units in six patients, 2 cat units in eight patients, and 3 cat units in two patients. The average for the group of twenty-eight patients to whom the drug was given was 1½ cat units (2¼ grains).

TABLE I

COMPARISON OF MAINTENANCE DOSAGE OF DIGITALIS AND OF GITALIN

CASES		GITALIN—		DIGITALIS—	
		DAILY DOSE IN GRAINS	AVERAGE APICAL RATE	DAILY DOSE IN CAT UNITS	AVERAGE APICAL RATE
1.	R. A.	1/120	78	1½	70
2.	J. B.	1/240	64	½	72
3.	M. B.	1/80	88	1½	86
4.	N. B.	1/240	72	1	74
5.	V. C.	1/120	86	1	88
6.	I. C.	1/80	86	3	88
7.	J. F.	1/240	72	½	68
8.	A. F.	1/120	72	1½	68
9.	I. G.	1/240	74	1	70
10.	D. G.	1/160	72	1½	76
11.	J. G.	1/240	82	1	74
12.	G. G.	1/100	86	1½	88
13.	F. G.	1/240	78	1	76
14.	H. I.	1/80	86	2	80
15.	L. K.	1/100	80	2	80
16.	R. K.	1/80	84	2	86
17.	I. K.	1/80	80	2	70
18.	H. L.	1/160	72	1	74
19.	S. P.	1/120	78	1	80
20.	S. P.	1/80	88	1	86
21.	G. R.	1/100	82	2	80
22.	K. S.	1/40	84	2	82
23.	D. S.	1/80	76	2	72
24.	L. S.	1/50	84	2	86
25.	R. S.	1/80	82	3	84
26.	S. W.	1/120	72	1½	72
27.	Y. W.	1/80	88	1	84
Average		1/110		1½	

The daily maintenance dose of gitalin was found to be 1/240 grain in six patients; 1/160 grain in four patients, 1/120 grain in nine patients, 1/100 grain in four patients, 1/80 grain in nine patients; 1/50 grain in one patient, and 1/40 grain in one patient. The average for the group of thirty-four patients to whom gitalin was administered was 1/110 grain. From a comparison of these maintenance doses of the two drugs, one may conclude that, clinically, 1/160 grain of gitalin is equivalent to 1 cat unit of digitalis. This is at variance with the observations of

Stroud and his associates,[3] who found that $\frac{1}{240}$ grain of gitalin was the clinical equivalent of 1 cat unit of digitalis (approximately $1\frac{1}{2}$ grains of the powdered leaves).

Table I shows that $\frac{1}{160}$ grain of gitalin and 1 cat unit of digitalis are not equivalent in every case (e.g., cases 6, 20, 22, 24, 25), but in any given case the ratio between the maintenance doses of the two drugs remains constant. We determined this by giving a patient first one drug, then the other, and then the first one again. We are unable at present to explain the variation in the equivalent doses of the two drugs. It may depend on differences in absorption, elimination, and duration of action. Patients in whom the equivalent doses departed markedly from the average exhibited some degree of heart failure during this whole study.

An additional complicating factor is the well-known fact that the digitalis requirements of different patients vary considerably, irrespective of the particular form of digitalis that is prescribed. In the present series of cases we reviewed the following factors in relationship to digitalis dosage: The size of the left auricle, the size of the left ventricle, previous attacks of heart failure, the degree of neurocirculatory imbalance, degree of heart failure present, and body weight. The cases are too few in number to allow of statistical deductions, but, as far as the figures go, no relationship between any of these factors and the size of the digitalis dose can be demonstrated. The only possible exception is that seven patients who weighed 160 lb. or more all required doses of digitalis larger than the average.

Of the twenty-nine patients who gave a statement relative to preference for either gitalin or digitalis, sixteen had no preference, six preferred gitalin, and seven preferred digitalis. The reasons for preference were not significant; some felt less tired, less dizzy, or less choked, on one or the other drug.

There was close correspondence between gitalin and digitalis in their effect upon the R-T segment and T-wave of the electrocardiogram. In eleven patients neither drug in therapeutic doses produced T-wave changes. In twelve patients both drugs produced slight T-wave changes, in ten patients moderate changes, and in two patients marked changes. There were insignificant discrepancies in only two patients.

Eight patients were studied in an attempt to compare the persistence of action of the two drugs. The heart rate was used as a measure of persistent digitalis effect. Gitalin was discontinued until the heart rate rose to 120 beats per minute or until the prior appearance of increased dyspnea, fatigability, distressing palpitation, or weight gain. Then digitalis was given, and, when the rate was again controlled, digitalis was withdrawn. The cases are too few and the results too variable to allow of categorical conclusions, but it is clear

that the gitalin effect lasted at least as long as digitalis, if not a bit longer. Haag,[9] working with pigeons, found persistence of action of five to ten days with tinctures of digitalis, and of about two weeks with gitalin.

Eight patients when first seen had been taking no digitalis and had rapid ventricular rates. The average rate was 138 beats per minute at the time of examination. These patients were given large doses of gitalin within a few days (average 2½ days). At the end of this period the average ventricular rate was 84 beats per minute. The average amount of gitalin that effected this slowing was $\frac{7}{80}$ grain. This, according to our other studies, is equivalent to 14 cat units of digitalis. This corresponds to general clinical experience with digitalis dosage[10] and also agrees with the observation by Stroud and his associates[3] that clinical improvement and slowing of the ventricular rate in untreated patients with auricular fibrillation are effected by a total dosage of $\frac{1}{16}$ to $\frac{1}{10}$ grain of gitalin. Baker and Bloom[11] also found that the quantity necessary for complete digitalization varies from $\frac{6}{80}$ to $\frac{10}{80}$ grain. Our results with rapid digitalization give further evidence that $\frac{1}{160}$ grain of gitalin is equivalent clinically to 1 cat unit of digitalis.

Luten[12] has recently claimed that in patients with auricular fibrillation without heart failure therapeutic doses of digitalis produce no slowing of the ventricular rate. This statement is at variance with our experience. We studied several patients who had been taking no digitalis and showed no clinical evidence of heart failure. In all of these cases the range of the ventricular rate was reduced rapidly from 118-160 beats per minute to 76-100 beats per minute by gitalin medication.

CASE 1.—E. F., a woman 46 years of age, with mitral stenosis, mitral insufficiency, and aortic insufficiency, had had auricular fibrillation for less than a year. She had not taken digitalis during the two weeks immediately preceding her office visit. On examination the lungs were clear, the liver was not enlarged, and there was no peripheral edema. The ventricular rate was 140 beats per minute. Fluoroscopic examination showed that there was moderate enlargement of the chambers of the heart. Within twenty-four hours she was given seven tablets (each 1/80 grain) of gitalin, and the ventricular rate was slowed to 76 beats per minute. There was no subsequent weight loss.

CASE 2.—N. B., a man 39 years of age, gave no history of rheumatic fever, but had known that he had a heart murmur for about twenty years. During these twenty years, he had experienced occasionally, and more frequently during the year immediately preceding, sudden attacks of palpitation and irregularity of the heart beat, lasting about forty-eight hours and ending abruptly. He had taken no digitalis for ten years, and had never taken any quinidine. He was examined the day after his last attack of palpitation. There was slight cyanosis of the lips. The lungs were clear. The liver was not enlarged. Fluoroscopically there was great enlargement of the left auricle and right ventricle and slight enlargement of the left ventricle. The first heart sound was sharp and was preceded by a diastolic

rumble. There was a diastolic murmur to the left of the sternum. The heart-beat was absolutely irregular, and the rate was 136 beats per minute. The blood pressure was 120/90. Within three days 1/10 grain of gitalin was given and the heart rate dropped from 140 to 76 beats per minute. The dose of gitalin was sharply reduced, but four days later the rate had dropped to 48 beats per minute. Except for the slowed apical rate there was absolutely no change in his physical findings, and no loss in weight occurred.

CASE 3.—M. B., male. At the age of 36 years, auricular fibrillation was discovered. There was no history of rheumatic fever or of a murmur. At the age of 39 years, when he was first examined at the office, the lungs were clear, and fluoroscopically there was considerable enlargement of the left ventricle. The heart sounds were of good quality. There were no murmurs. Auricular fibrillation was present, and the ventricular rate was 80 per minute. (He had been taking some digitalis in the preceding few days.) The blood pressure was 138/100. During the next five years he worked steadily as a painter. There was slight dyspnea on walking seven blocks. He continued to take small amounts of digitalis irregularly. When examined again, at the age of 44 years, the lungs were clear and the liver was not enlarged. Fluoroscopically there was considerable enlargement of the left ventricle and moderate enlargement of the left auricle. The first heart sound was of good quality. There were no murmurs. The apical rate varied from 84 to 100 beats per minute. The blood pressure was 125/100. He was given gitalin, and his heart rate was maintained between 80 and 90 on 1/80 grain daily. The drug was then withdrawn for twenty-four days. At the end of this time the apical rate had risen to 112 beats per minute, and he noted some increase in dyspnea on climbing stairs. On a standard exercise tolerance test his apical rate increased from 112 to 122 beats per minute. The circulation time (when the heart rate was 112 per minute) was 17.5 sec. by the decholin method.[13] To physical examination his condition was unchanged. The lungs were clear, the liver was not enlarged, there was no peripheral edema, and there had been no increase in weight. He was then given 2 cat units of digitalis a day for one week. At the end of this period his heart rate was 74 beats per minute. His condition was still unchanged, and there had been no weight loss.

CASE 4.—One of us[14] reported in a previous communication the case of a woman, 50 years of age, with Graves' disease of two years' duration. There was sweating, tremor of the hands, and progressive weight loss. Irradiation of the thyroid gland by means of radium had been ineffectual. There was considerable enlargement of the left ventricle, and auricular fibrillation was present. The basal metabolic rate was + 65 per cent. The heart rate was recorded by means of the cardiotachometer both before and after digitalization (the patient received 61 c.c. of the tincture of digitalis in sixteen days). The resting rate before digitalis was given was approximately 116 beats a minute, as compared with 98 per minute after digitalization. There had been no subjective or objective evidence of heart failure before digitalization.

When gitalin was withdrawn from several of the patients the ventricular rates rose from approximately 80 to an average of 112 beats per minute; no clinical evidence of heart failure was found at these high rates. When digitalis was then administered, the rates were again slowed to the same degree. Of eight cases, in which withdrawal of one or the other drug caused increases in ventricular rate without concomitant clinical evidences of heart failure, the circulation

time was measured in six, both before and after digitalization, using the decholin method. The results are shown in Table II. In none of these six cases was there any significant change in the circulation time when the ventricular rate was rapid and the patient was not under the influence of digitalis. Observation both of untreated patients and of those from whom the drug could be withdrawn at will indicates that, in many cases at least, the increased ventricular rate is not due to heart failure and that it can be readily slowed by appropriate doses of digitalis. These clinical studies do not substantiate Luten's contention that slowing by digitalis of the ventricular rate in auricular fibrillation is effected only when heart failure is present.

It seems logical at this point to question the value of slowing the ventricular rate if no heart failure ensues because of the rapid rate. However, patients feel much better with slower rates, notice less palpitation on slight or moderate exertion, and do not experience the throbbing and violent palpitation on exertion or emotion that occur in those with uncontrolled auricular fibrillation. Even at rest the uncontrolled rapid rate is distressing and makes patients more heart-conscious.

TABLE II

CIRCULATION TIME STUDIES IN PATIENTS, DIGITALIZED AND UNDIGITALIZED

PATIENT	DIGITALIZED		UNDIGITALIZED	
	CIRCULATION RATE IN SECONDS	APICAL RATE	CIRCULATION RATE IN SECONDS	APICAL RATE
R. A.	18.5	66	17.5	106
I. G.	16.5	60	15.5	72
S. P.	15.0	80	14.0	88
F. G.	21.0	86	22.0	106
I. K.	13.5	72	15.0	90
H. L.	18.0	72	19.0	100

H. I., male, gave no history of rheumatic fever, but at the age of 45 years his application for life insurance had been rejected because of a murmur. At the age of 50 he had had an attack of palpitation with rapid heart rate, lasting three days. When he was examined a week after this attack, auricular fibrillation was present, and the ventricular rate was 160 beats per minute. There was extreme enlargement of the left auricle and both ventricles. The blood pressure was 125/100. The lungs were clear and the liver not enlarged. Unusually large doses of gitalin, administered over a period of weeks, were required to reduce his heart rate to a range of 72 to 84 beats per minute. He had been afebrile. His basal metabolic rate was −15 per cent. The sedimentation time of the red blood cells was over one hour for 18 mm. Once controlled, he was maintained adequately on 1/80 grain of gitalin, and subsequently on 2 cat units of digitalis. When he was digitalized, he experienced no racing of the heart on exertion. He was able to walk considerably more, and stair climbing induced less dyspnea; yet he exhibited no manifest heart failure when his ventricular rate was rapid.

In patients with auricular fibrillation but without heart failure the uncontrolled rapid irregular rate acts as a mechanical embarrassment

to an already damaged heart. Rapid rates, regular or irregular, may produce no symptoms when the myocardium is normal, but persistent rapid rates are injurious to diseased hearts. Enlarged hearts, in particular, are more likely to fail when their beating is persistently rapid.[15] Even in patients with auricular fibrillation whose ventricular rates are relatively slow when they are at rest, it is best to administer small doses of digitalis, because exertion then provokes less discomfort, palpitation, and acceleration of the heart rate.

TOXIC REACTIONS

Overdosage with gitalin produces toxic effects similar to those produced by overdosage with whole leaf digitalis preparations.[3] Toxic reactions and untoward effects during digitalis administration are singularly few when the drug is used with care. On only a very few occasions in the present study were mild toxic symptoms encountered with either drug—nausea in a few patients and extrasystoles in two patients. Even in the group in which large doses of gitalin were administered to effect rapid slowing of the ventricular rate, no toxic symptoms were encountered. In using either drug, one must constantly keep in mind the great individual variations in maintenance dosage, and ascertain by experiment the proper amount for each patient. Dosage according to body weight serves as a rough guide in treating the acutely ill, but it is unreliable when the drug must be given for long periods of time. On very rare occasions, digitalis cannot be taken by mouth. Rectal administration is often efficacious in such cases. Digitalis products may be dispensed in colored capsules for patients who have developed an aversion to the use of green digitalis tablets. In such cases, too, the administration of a white digitalis preparation, such as gitalin, is equally effective.

SUMMARY

A comparative study of the actions of gitalin and digitalis was made in thirty-six ambulant patients with auricular fibrillation.

Gitalin acts like digitalis in slowing the ventricular rate and relieving congestive heart failure in patients with auricular fibrillation.

Gitalin parallels digitalis in its effect on the R-T transition and T-waves of the electrocardiogram.

Gitalin has a persistence of action at least as long as digitalis.

Rapid administration of gitalin in eight patients produced prompt and effective slowing of ventricular rates and clinical improvement without the development of toxic symptoms.

The average daily maintenance dose of gitalin was $\frac{1}{110}$ grain; of digitalis, $2\frac{1}{4}$ grains, or $1\frac{1}{2}$ cat units.

Clinically, $\frac{1}{160}$ grain of gitalin is equivalent to 1 cat unit of digitalis leaves.

The daily maintenance dosages of both drugs show considerable variations in different individuals.

Toxic reactions to gitalin are the same as to digitalis. They are neither more nor less frequent. With careful administration they should be rare with either drug.

Our studies indicate that digitalis can slow ventricular rates in auricular fibrillation in the absence of heart failure, which is contrary to the contention that slowing of the ventricular rate in auricular fibrillation is effected by digitalis only in the presence of heart failure.

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ANGINA PECTORIS AND MYOCARDIAL INFARCTION AS COMPLICATIONS OF MYXEDEMA

With Especial Reference to the Danger of Treatment With Thyroid Preparations*

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MYXEDEMA complicated by angina pectoris has been observed frequently, but a fatal outcome resulting from myocardial infarction during treatment with thyroid is rare. As far as could be determined only eight such cases have been reported, and in only five of these was the diagnosis confirmed at autopsy. The purpose of this communication is to review these previously reported cases and to record one additional case.

Numerous observers (Christian,[1] Sturgis,[2] Sturgis and Whiting,[3] Fahr,[4] Abrami and co-workers,[5] and Gordon[7]) have warned of the dangers encountered in the use of desiccated thyroid gland in the treatment of patients with myxedema, especially when cardiac symptoms are present. Because of the widespread use of this substance in mild hypothyroid states and the recent production of artificial myxedema as a mode of treatment in myocardial failure and angina pectoris (Blumgart, Levine, and Berlin[8]), it seems timely to re-emphasize the need for caution in the administration of this drug and to stress the importance of watching for signs of cardiac failure when it is used.

REVIEW OF THE LITERATURE

The occurrence of cardiac pain in myxedema was first reported by Hertoghe,[9] in 1914; he attributed it to a myxedematous change in the nerve cells of the connective tissue of the heart. Zondek,[10] who introduced the term "myxedema heart," mentioned pain in myxedema but gave no details concerning its type or distribution. In 1924, Laubry, Mussio-Fournier and Walser[11] reported the first case of true angina pectoris associated with myxedema. They thought that arteriosclerosis played a part in the production of the pain but that it was largely "functional" in origin. The first American account of this complication was published by Christian[1] in July, 1925. The patient was a woman, 50 years of age, with severe constricting pain in the chest, of one year's duration, which had the typical radiation of angina pectoris. The basal metabolic rate was –32 per cent. After taking 0.52 gm. of thyroid daily for four days she developed circulatory failure. There was temporary

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recovery following reduction of the dose to 0.13 gm. daily, but later she went into shock and died of coronary occlusion sixteen days after the treatment was instituted. This case is particularly interesting because it closely parallels the one reported herein.

Fahr,[12] who reported the first cases of myxedema heart in this country, found one man, 49 years of age, who had occasional attacks of precordial pain on exertion. This symptom disappeared after five months' treatment with desiccated thyroid. Since that time other observers have noted the improvement or disappearance of angina following thyroid therapy (Chapman,[13] Higgens,[14] Ziskin[15]). Gordon,[7] on the other hand, had one patient, a woman 62 years of age, who developed angina following the injection of 10 mg. of thyroxin. He also observed a man who developed precordial pain which radiated down both arms while under treatment for hypothyroidism with 0.32 gm. of desiccated thyroid gland daily.

The difficulty of treating a patient who has both myxedema and heart disease has frequently been observed. Escimilla[16] reports a case of myxedema illustrating this problem. The patient had had chest pain for three years. A dose of 0.065 gm. of desiccated thyroid was not tolerated because of angina, and therefore the dose was gradually reduced to 0.015 gm. once per week, but even with this small amount some localized pain over the heart continued.

Little attention has been paid to the association of angina or myocardial infarction with myxedema. In 1925, Willius and Haines,[17] in a report of 162 cases of high-grade myxedema, observed only one patient with angina. The following year, Means, White, and Krantz,[18] in reviewing 48 cases of myxedema, found one patient who developed twinges of pain following the use of thyroid in doses of 0.12 gm. per day. One of Lerman, Means and Clark's[19] 18 patients with myxedema suffered from angina before thyroid medication was started and died at home, probably of coronary occlusion. In the following series of cases of myxedema there is no mention of cardiac disease: Case[20] (58 cases), Lawrence and Rowe[21] (120 cases), Riecker[22] (64 cases). All accounts of either angina pectoris or coronary occlusion complicating myxedema are isolated instances and so give no indication of the incidence of this combination of diseases.

Wegelin[23] and Ohler and Abramson[24] have called attention to the fact that little autopsy material is available for the study of myxedema. The following are summaries of all of the cases of myxedema and myocardial infarction due to coronary occlusion in the American literature.

CASE 1.—Christian,[1] in 1925, and Sturgis and Whiting,[3] in 1926, reported a case of myxedema and angina pectoris in a woman 50 years old. Her treatment consisted of 0.13 gm. of dried thyroid gland three times a day for two days, then 0.13 gm. four times a day for two days. The drug was discontinued when she developed cyanosis, a feeble pulse, and other signs of acute cardiac failure. Recovery fol-

lowed, and on the sixteenth hospital day treatment was resumed with 0.03 gm. of thyroid three times a day, but death occurred forty-eight hours later. Autopsy showed coronary atherosclerosis, cardiac infarction, hypertrophy and dilatation of the heart, atrophy and fibrosis of the thyroid gland, and generalized atherosclerosis.

CASE 2.—Fahr,[4] in 1932, reported a case in a woman aged 46 years who gave a history of hoarseness, slowness of speech, sluggishness, loss of memory, depression, dryness of the skin, and coldness of the hands and feet, all of two years' duration. She had had several attacks of severe precordial pain which usually came on after exertion and was relieved by rest. The basal metabolic rate was -25 per cent. She was advised to take 0.065 gm. of thyroid extract twice a day. Six days later she returned extremely nervous and apprehensive, saying that she had taken very little of the drug. She had experienced one attack of angina which was not relieved by morphine. In the hospital she received 0.13 gm. of desiccated thyroid daily. Another attack occurred on the eleventh hospital day, and thereafter, until her death three months later, angina occurred every day. Autopsy was limited to the heart, which weighed 475 gm. and showed almost complete occlusion of the left descending branch of the coronary artery with a fresh thrombus in its lumen. The other two branches were narrowed. There was necrosis of the heart muscle, indicating that the accident must have occurred a few days before death.

CASE 3.—Means and Lerman,[25] in 1935, gave an account of a housewife, 52 years of age, who for two or three years prior to entry had slowly been developing symptoms characteristic of myxedema. Her basal metabolic rate was reported to be low. Thyroid was taken in full doses (0.3 gm. tablets, one and one-half tablets the first day, two tablets the second day, two and one-half the third day, and three tablets per day thereafter), whereupon she developed massive edema of the extremities, swelling of the abdomen, marked dyspnea and orthopnea, and some precordial aching. Both she and her doctor were sure that the thyroid produced these symptoms, and it was therefore discontinued. On admission, examination revealed signs of myxedema and cardiac failure. The basal metabolic rate was normal because of the thyroid that she had received. It was thought that she had heart disease, probably rheumatic, with mitral regurgitation. On full doses of digitalis the cardiac symptoms improved, and the basal metabolic rate fell to -32 per cent. She was discharged, and returned four months later with fully developed myxedema but no signs of decompensation. Thyroid was administered in doses of 0.032 gm.; it was well tolerated and relieved the myxedematous manifestations. The third admission was because of recurrence of the dropsy. The patient died very suddenly. Autopsy showed that the thyroid was atrophic. The heart weighed 600 gm. The right ventricle was dilated and hypertrophied. The changes in the mitral valve were such as to produce regurgitation but not stenosis. Both coronary arteries showed lesions. In the left there were calcification and fibrosis; the lumen was reduced to about one-half of its normal caliber and at one point was narrowed still further by a fresh red thrombus. The right coronary showed narrowing and thickening but no calcification. It was thought that the immediate cause of death was a fresh coronary occlusion and that the myxedema, by diminishing the work of the heart, probably postponed death rather than hastened it.

CASE 4.—Higgens,[14] in 1936, reported a case in a woman, 53 years of age, who was admitted complaining of weakness. She was mentally sluggish and had a dry skin. The basal metabolic rate was -28 per cent. There was complete remission of symptoms after thyroid therapy. Her last illness followed a two months' interruption of treatment. She entered with signs of cardiac failure. Improvement followed treatment with thyroid, but while still in bed she developed precordial pain which was followed later by symptoms of coronary occlusion. Autopsy showed that the heart

was somewhat hypertrophied, that all of the coronaries were much thickened, and that the left ventricular wall was very thin and composed of fibrous tissue. Microscopically the myocardial changes were such as are commonly found in patients with coronary atherosclerosis.

CASE 5.—In the same paper Higgens[14] gives an account of a woman, 55 years of age, who complained of weakness and swelling of the extremities. With the exception of the basal metabolic rate, which was -33 per cent, the examination was negative. Her symptoms disappeared under thyroid therapy. Four months before her second admission to the hospital she suffered an attack typical of coronary occlusion, from which she made a slow but satisfactory recovery. The symptoms at the time of her second admission were dyspnea, swelling of the legs, and weakness. Examination revealed enlargement of the liver, which extended a hand's breadth below the costal border, and signs of fluid at the bases of both lungs. Her death was apparently caused by progressive coronary disease. Autopsy revealed extremely sclerotic coronaries, with reduction of their lumina to pin-point size. The apical half of the left ventricular myocardium was almost completely replaced by fibrous tissue, which was about one-eighth of an inch thick at the apex.

In addition to these five cases of myxedema and myocardial infarction in which autopsies were performed, clinical reports of three cases of myxedema in which sudden death followed thyroid therapy have been published.

Graves,[26] in 1927, treated a woman 54 years of age who had symptoms of myxedema and a basal metabolic rate of -40 per cent. After taking 1 gm. of desiccated thyroid daily for three days she developed symptoms of coronary occlusion and died. Lerman, Means, and Clark[19] observed a man, 55 years of age, with angina pectoris and a basal metabolic rate of -29 per cent. The electrocardiogram showed bundle branch block. Although the authors made no statement regarding therapy, it may be assumed that the patient was treated with thyroid. A year later he died suddenly at home, probably of coronary occlusion. Ohler and Abramson's case[24] was that of a man, 30 years of age, who had a basal metabolic rate of -21 per cent and edema of the lower extremities. He received 0.972 gm. of desiccated thyroid daily, and the edema disappeared; but four days after he was discharged from the hospital, he suddenly complained of severe pain in the left shoulder, dropped to the floor, and died half an hour later. The authors were of the opinion that his death was due to coronary occlusion, and that the latter was at least partly the result of excessive doses of thyroid.

The following is an additional case of myxedema and angina pectoris. The patient died of myocardial infarction on the eighth day of treatment with desiccated thyroid.

REPORT OF CASE

History.—L. C., a woman 63 years of age was admitted to the Medical Service of the University of Michigan Hospital March 8, 1937, complaining of fatigability, listlessness, and pain in the upper right quadrant of the abdomen and around the heart. The abdominal pain had been periodic and colicky, and radiated along the right costal margin to the right scapula. Jaundice had been noted with some of the attacks. Five years earlier she had begun to notice that she was becoming sluggish and was articulating with difficulty and that her hair seemed dry, her voice husky

and her face and eyelids puffy. At that time she was told that she would have to take thyroid the remainder of her life. Treatment helped her, but she had taken no thyroid for two years prior to admission, and not only had all of her original symptoms returned, but, in addition, she had developed retrosternal pain, attended with a sense of weight on the chest, which was brought on by exertion and at times radiated down both arms. Rest and nitroglycerin had given immediate relief.

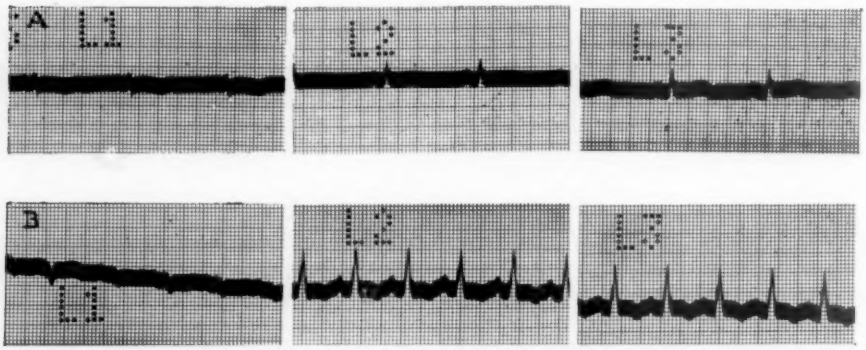

Fig. 1.—*A*, before treatment. *B*, day of death.

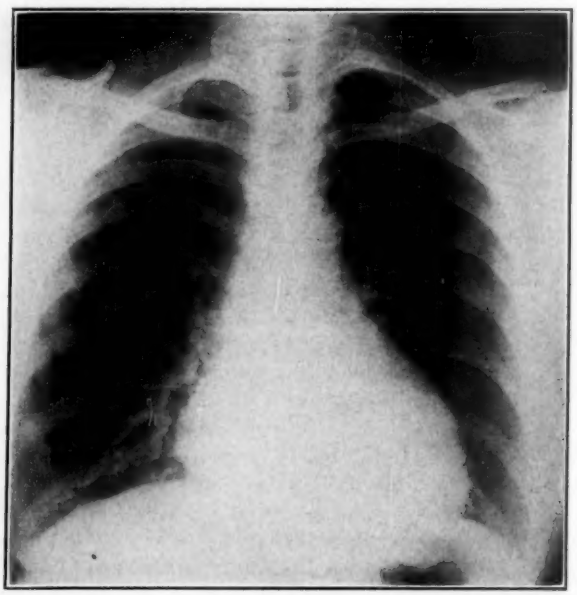

Fig. 2.—Moderate generalized cardiac enlargement.

Physical Examination.—The patient appeared to be chronically, but not acutely, ill. Her speech, motions, and response to questions were slow. The skin was pale, dry, and scaly. The hair on the arms, in the axillae, over the pubes, and in the eyebrows was scanty. Her face was oval, her eyelids puffy, and her lips thick. The heart was enlarged, with the left border of dullness 11 cm. to the left of the mid-sternal line. The blood pressure was 108/80.

Laboratory Examination.—The blood Kahn reaction was negative. The urine was normal. The hemoglobin was 57 per cent (Sahli); the erythrocytes numbered

3,200,000, and the leucocytes 6,800 per cubic millimeter. The differential leucocyte count was normal. There were 540 mg. of cholesterol per 100 c.c. of blood. On two occasions the basal metabolic rate was -41 per cent, and -37 per cent, respectively. The electrocardiogram before treatment was started (Fig. 1*A*) showed a heart rate of 62 per minute, with very small complexes and inverted T-waves in Lead I. A tracing taken six or eight hours before death (Fig. 1*B*), when the heart rate was 111 per minute, showed very bizarre QRS complexes in Lead I and fairly large, notched, upright QRS waves in Leads II and III. The QRS interval was slightly prolonged (0.11 sec.). The curve suggested partial right bundle branch block. Roentgenologic examination of the chest revealed moderate enlargement of all four chambers of the heart (Fig. 2). Measurements of the frontal plane area and transverse diameter of the heart by means of the orthodiagram and teleoroentgenogram agreed closely. When compared with the Eyster-P. C. Hodges tables, it was found that in the orthodiagram the frontal plane area was increased by 34 per cent, and the transverse diameter by 26 per cent; and that in the teleoroentgenogram the former was increased by 38

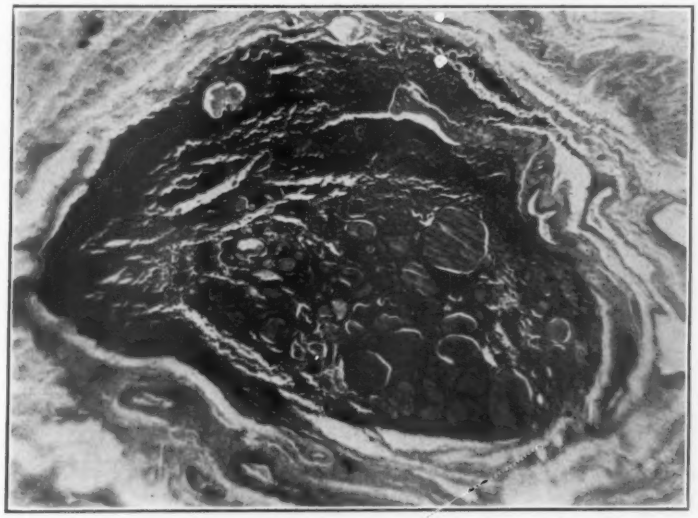

Fig. 3.—Largest nodule found in the thyroid gland.

per cent, and the latter by 23 per cent (a variation of 12 per cent above or below the calculated average is not considered abnormal).

Course in Hospital.—During the first few days the patient's temperature was subnormal. She was ambulatory and comfortable. On the second hospital day she received 0.12 gm. of desiccated thyroid, and 0.26 gm. daily for four days thereafter. Two days after treatment began she noticed a feeling of increased warmth, her temperature returned to normal, and she felt much better. On the third day the patient experienced typical anginal pain which was relieved by nitroglycerin. The two subsequent days were marked by an increase in the frequency and severity of the anginal attacks. The dose was then reduced to 0.065 gm. per day, and the drug was discontinued on the seventh day, after a total of 1.5 grams had been given. On the morning of the eighth day after the institution of thyroid therapy the precordial pain became constant and was not relieved by nitroglycerin or codeine and only slightly by morphine. The patient developed nausea, vomiting, cyanosis and extreme dyspnea; her pulse became imperceptible; her blood pressure fell so low that it

could not be measured; and râles appeared throughout both lungs. She died in the evening of the same day, fifteen days after admission.

Autopsy.—The thyroid showed diffuse atrophy with marked lymphocytic infiltration. The largest nodule in the thyroid gland is shown in Fig. 3. The heart weighed 190 gm.; its walls were soft and flabby. The coronary arteries were narrowed by extensive atherosclerosis and calcification. In the anterior and posterior branches of the left coronary there was a progressive narrowing as the apex was approached. There were both old and recent myocardial infarcts. One of the most recent was of large size, was surrounded by an active leucocytic infiltration, and appeared to be three or four days old (Fig. 4). No thrombosis or embolism was found. Massive pulmonary edema was present. The aorta showed atherosclerosis. It is of interest in view of the history of pain in the upper right quadrant which radiated to the scapula that there was no evidence of chronic cholecystitis.

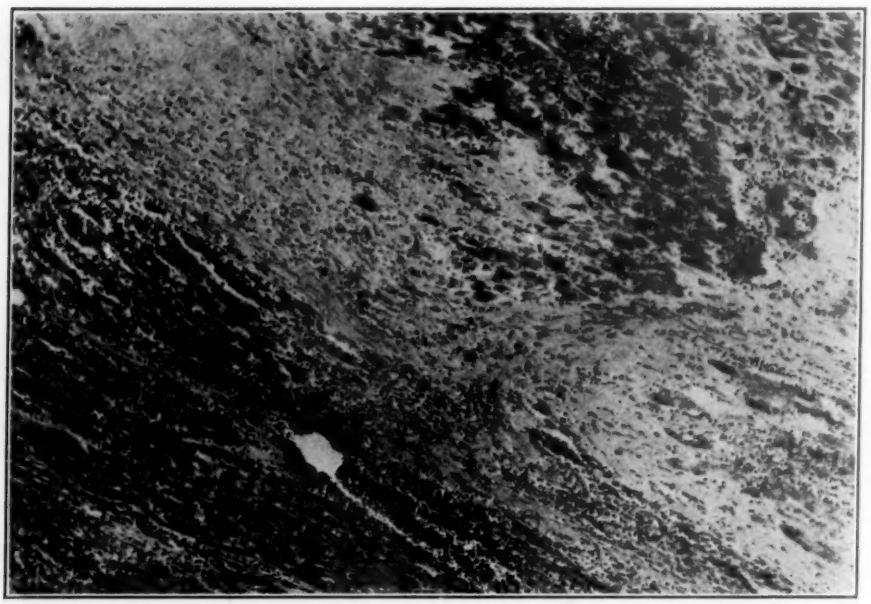

Fig. 4.—Area of myocardial infarction showing necrosis and leucocytic infiltration.

DISCUSSION

Narrowing of the coronary arteries was found in our case and in all other reported cases in which an autopsy was performed. Bournville[27] and Fishberg[28] have produced evidence that there is a high incidence of arteriosclerosis in myxedema. The experiments of von Eiselsberg[29] on sheep and goats and of Shapiro[30] on rabbits showed that thyroidectomy predisposes to atherosclerosis. This may be related in some way to hypercholesterolemia, which is constant in myxedema, and is regarded by some as a valuable index of thyroid underactivity. Our patient's blood cholesterol level was high (545 mg. per 100 c.c.).

At present we have no way of judging how frequently patients with myxedema develop myocardial infarction, or whether the occurrence of angina pectoris and arteriosclerosis is more common in these patients

than in others of the same age. When the 108 proved cases of myxedema* which were seen in the University of Michigan Hospital between January, 1930, and March, 1937, were reviewed, it was found that angina pectoris had been present in two. The case reported herein is the only one of this series in which (1) the clinical diagnosis of myxedema was confirmed by metabolic studies and (2) an autopsy was performed. During this period of six years and two months the incidence of myxedema was 1 to 1313.

It has recently been shown that the administration of thyroid increases the blood velocity and the minute output of the heart; thus the myocardium must be supplied with more blood, and therefore it is reasonable to suppose that in our patient the narrowed coronary arteries were inadequate. As a result of this, it could be assumed that a localized area of necrosis of the myocardium developed. The acute cardiac failure was not associated with coronary thrombosis, and in only two of the five reported cases in which an autopsy was performed was thrombosis demonstrated.

It may be argued that in this case and in those previously reported, in all of which advanced atherosclerosis of the coronary arteries and angina pectoris were present, myocardial infarction might have developed had no thyroid substance been given at all. As Davis[31] has aptly said, "One does not have to have myxedema to die of coronary thrombosis." It may well be that what we have observed is merely a coincidence, but it is nevertheless apparent that the number of reported cases of death from myocardial insufficiency in patients with untreated myxedema is remarkably small. Perhaps as the number of autopsies in cases of myxedema increases and more careful follow-up studies are reported, the frequency of this combination of diseases will be found to be significantly higher than our present records would indicate. At present we may conclude that a fatal outcome during active treatment is sufficiently common to justify repetition of the warning against the indiscriminate use of thyroid gland products, especially when the patient has retrosternal pain or other possible signs of heart disease.

SUMMARY

1. A review of the literature dealing with myxedema complicated by angina pectoris and myocardial infarction disclosed five cases in which autopsy showed that death was caused by acute coronary failure. These cases are summarized.

2. One case of myxedema and angina pectoris in which myocardial infarction developed during treatment with thyroid substance is reported.

3. Before giving thyroid gland products, a careful estimate of the cardiovascular status is necessary.

*There were 11 additional cases in which either the clinical manifestations were not well marked, or the clinical diagnosis was not substantiated by measurement of the basal metabolic rate.

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INCIDENCE AND TYPE OF HEART DISEASE IN SAN FRANCISCO SCHOOL CHILDREN*

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FOR the purpose of determining the incidence and type of heart disease in San Francisco school children, we have analyzed (1) the records of the Cardiac Diagnostic Center of the San Francisco Department of Public Health and (2) data obtained from study of a sample of the San Francisco school population.

STUDY OF TYPES OF HEART DISEASE OBSERVED AT THE CARDIAC DIAGNOSTIC CENTER

The present analysis of data obtained in the Cardiac Diagnostic Center covers a three-year period and makes use of the facilities described in Richter's report.[1] In that report it was explained that all school children are examined routinely by trained pediatricians of the San Francisco Department of Public Health. All cardiac suspects are referred either to their own physicians or to the Cardiac Diagnostic Center, which is administered by the Department of Public Health.

Roentgenographic, fluoroscopic, and electrocardiographic facilities are available. Regular follow-up investigations are made by members of the school nursing department, and these assist materially in ultimately obtaining accurate diagnoses. All cardiac disease suspects are examined by staff members on at least two visits, and many of the children included in our series were examined at six-month intervals throughout the three-year period. The criteria for diagnosis are those established by the American Heart Association.†

Statistical data are used in this study because, until rheumatic fever and its manifestations are made reportable, they afford the most satisfactory index of morbidity rates.

Table I is composite, showing the number of examinations made during each of the three years in the San Francisco schools and in preschool and well-baby conferences. Murmurs, fainting attacks, pulse irregularities, tachycardia, and hypertension are some of the symptoms for which these children are referred.

Table I also presents the diagnoses made by members of the staff of the Cardiac Diagnostic Center. It should be noted that although the number of children referred decreased over the three-year period,

*From the San Francisco Department of Public Health, and the Departments of Medicine and of Pediatrics of the University of California Medical School.
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†The San Francisco Cardiac Diagnostic Center is affiliated with the American Heart Association.

TABLE I

ANALYSIS OF DIAGNOSES MADE BY THE STAFF OF THE CARDIAC CENTER, 1931-1934

	1931-1932		1932-1933		1933-1934	
Total school and preschool examinations	55,679		51,555		52,227	
Types of lesions	*no.*	*% of total no. of suspects*	*no.*	*% of total no. of suspects*	*no.*	*% of total no. of suspects*
Organic	162	29.4	98	21.8	61	20.9
Functional	179		137		151	
Noncardiac	110		34		47	
Diagnosis deferred	98		87		33	
Total new heart disease suspects examined	549		356		292	

the percentage of cases of organic heart disease among them remained remarkably constant.

Table II contains analyses of cases in which the examinations were made by one of the authors (Christie), of corresponding data from the investigation made in 1931 by Richter[1] at the same Cardiac Diagnostic Center, and of data obtained by Christie at the Children's Cardiac Clinic of the University of California.

TABLE II

TYPES OF ORGANIC LESIONS: COMPARISON OF INCIDENCE IN TWO SERIES STUDIED AT THE CARDIAC DIAGNOSTIC CENTER AND ONE SERIES AT THE UNIVERSITY OF CALIFORNIA CHILDREN'S HEART CLINIC

	TOTAL PATIENTS EXAMINED	TOTAL ORGANIC	TOTAL CONGENITAL	TOTAL RHEUMATIC	OTHER ETIOLOGY	PERCENTAGE OF CONGENITAL AMONG TOTAL ORGANIC
Cardiac Diagnostic Center (Christie, present report)	485	157	91	60	6	57.9
Cardiac Diagnostic Center (Richter[1])	483	319	140	151	28	43.8
Children's Heart Clinic of the University of California* (Christie[8])	143	94	36	54	4	38.3

*Unselected patients referred to the Children's Heart Clinic, most of them for follow-up after hospital admission.

The 485 patients (Table II) examined personally in the Cardiac Diagnostic Center by one of the authors (Christie) were unselected and were studied in successive groups of 100 cases. The incidence of congenital heart disease in the entire group of cases of organic heart disease varied between 64.4 per cent in the first 100 and 51.5 per cent in the second 100; the average of the entire group was 57.9 per cent.

It should be noted that the percentage of cases of congenital heart disease among the cases of organic heart disease in the series from

the Children's Heart Clinic of the University of California (38.3 per cent) is lower than that in the two other series. This is undoubtedly due to the fact that a large number of the patients followed in this clinic are referred from the Pediatric Service of the University of California Hospital, where they have been observed during and after attacks of acute rheumatic fever. It is significant that in this group congenital heart disease constituted 38 per cent of the organic lesions.

Another probable explanation of the fact that the incidence of congenital cardiac disease in the patients examined at the Cardiac Diagnostic Center was higher than in those at the Children's Clinic of the University of California is that the former were, on an average, younger than the latter. For the same reason, in the study of a more representative cross section of the entire school population reported in the second portion of this paper, the figures obtained agree closely with those from the Children's Clinic of the University of California, but not with those from the Cardiac Diagnostic Center (Table III). The distribution by age groups illustrating this changing differential is presented later in Table VI and is likewise clearly shown in the integral graphic chart of heart disease based on a survey of the entire city by Geiger, Sampson, Miller, and Gray[2] (Fig. 1).

As Eastern authorities [3-6] report that the incidence of congenital heart disease is 10 to 20 per cent of the organic lesions in their school populations, the high incidence of congenital cardiac disease in all three of the series shown in Table II gives evidence that there is a significant difference in the types of heart disease found in the eastern and western sections of the United States, provided similar diagnostic methods have been used in both regions. At the time our study was being made, we recognized this geographic discrepancy in incidence and therefore included in the congenital heart disease group only those cases in which the diagnosis was beyond question.

If we grant that congenital heart disease is due to a defect in germ plasm, there is no valid reason why it should occur more frequently in San Francisco than in any other locality. Since two observers working in three different clinics have noted an amazingly high percentage of congenital heart lesions in the groups of patients with organic heart disease, it seems logical to conclude that the incidence of rheumatic heart disease in this region is correspondingly low.

STUDY OF INCIDENCE FROM SAMPLING OF POPULATION

In the investigation of the group of cases reviewed above, no accurate estimate could be made of the actual incidence of cardiac disease in this particular unit of child population. This was due to the fact that it was impossible to determine how many of the school children with heart disease had been referred to the Cardiac Diagnostic Center

for study. Fifty per cent was considered a reasonable estimate both by Richter and ourselves (see footnote 2, Table VII).

The following study of a sample of population was made chiefly for the purpose of eliminating error in estimating the incidence of heart disease in the total population.

Following the method of sampling used by Cahan[7] and others, 295 children in 30 of the 135 San Francisco schools, including one "health school" for handicapped children, were examined personally by one of the authors (Sampson). The total school population in San Francisco at the time of this study was 87,324. The 295 children examined had been selected by trained pediatricians during routine complete physical examinations of 18,607 children, i.e., the total number of pupils registered in the 30 schools. For various reasons, the incidence in 4 of the schools, including the health school, could not be accurately determined. Therefore, further selection was made of 197 children from the 13,338 pupils registered in 26 schools; this series represented, with possibly rare exceptions, all of the suspected cases of heart disease in this group.

While many of the children in the group had been examined in the School Cardiac Diagnostic Center in the Department of Public Health Building, or by private physicians, there were many others who had never been examined except in the school building during class hours. It is recognized that the possibility of error in diagnosis in difficult cases is greater when only the ordinary means of physical examination are used than when the roentgen ray and the electrocardiograph may also be employed. Furthermore, errors are likely to occur in all statistical analyses of groups of cases diagnosed without confirmation by autopsy, and the data must therefore be evaluated accordingly.

In our opinion, the figures on incidence, given in Table III, among the 197 children from 26 schools, are based on reasonably accurate diagnoses. These figures therefore represent at least a minimal estimate of the percentage of cardiac patients in the total school population. The individuals were students in the primary, intermediate, and high school grades, and ranged in age from 6 to 18 years. The incidence of organic heart disease in this group was 13 cases per thousand.

TABLE III

INCIDENCE OF CONGENITAL AND RHEUMATIC HEART DISEASE IN 197 CARDIAC DISEASE SUSPECTS FOUND AMONG 13,338 SCHOOL CHILDREN

SCHOOL POPULATION REPRESENTED	HEART DISEASE SUSPECTS	ORGANIC HEART DISEASE	RHEUMATIC		CONGENITAL		RATES PER 1,000 SCHOOL POPULATION		
			TOTAL	%	TOTAL	%	ORGANIC	RHEUMATIC	CONGENITAL
13,338	197	49	30	62	19	38	3.7	2.2	1.4

TABLE IV

DISTRIBUTION OF CASES OF VARIOUS TYPES OF HEART DISEASE BY AGE GROUPS IN 295 CARDIAC DISEASE SUSPECTS AMONG 18,607 SCHOOL CHILDREN

AGE GROUPS INCL. (YR.)	POSITIVE DIAGNOSIS OF ORGANIC HEART DISEASE						DOUBTFUL DIAGNOSIS OF ORGANIC HEART DISEASE						POTENTIAL RHEUMATIC		HYPER-TENSION		FUNCTIONAL MURMURS OR ARRHYTHMIAS		TOTAL CARDIAC SUSPECTS
	RHEUMATIC		CONGENITAL		TOTAL		RHEUMATIC		CONGENITAL		TOTAL								
	TOTAL	%	TOTAL	%	TOTAL	%	TOTAL	%	TOTAL	%	TOTAL	%	TOTAL	%	TOTAL	%	TOTAL	%	
6-9	6	11.8	5	9.8	11	21.6	3	5.9	4	7.8	7	13.7	4	7.8			29	56.9	51
10-12	12	14.1	10	11.8	22	25.9	7	8.2	6	7.1	13	15.3	7	8.2	2	2.4	41	48.2	85
13-15	18	21.3	10	12.0	28	33.3	6	7.2	7	8.3	13	15.5	4	4.8	2	2.4	37	44.0	84
16-18	12	16.2	5	6.8	17	23.0	4	5.4	1	1.4	5	6.8	3	4.0	7	9.5	42	56.7	74
19	1	100.0			1	100.0													1
Total	49	16.6	30	10.2	79	26.8	20	6.8	18	6.1	38	12.9	18	6.1	11	3.7	149	50.5	295

The 295 cases of possible cardiac disease among 18,607 school children, which are analyzed in Table IV, include the group of children in the health school where a high percentage of the pupils registered are cardiac patients who have, for this reason, been selected for placement in this school. Such a concentration of cases does not affect the study of relative incidence of types of organic disease in this series of cases, but it does increase the apparent incidence of heart disease in the school population as a whole.

Table IV shows the comparative frequency of congenital and rheumatic heart disease, hypertension, and potential rheumatic and doubtful cardiac disease in various age groups. With the exception of two individuals, the groups covered inclusively the ages of 6 to 9, 10 to 12, 13 to 15, and 16 to 18 years. One child in the series was 5 years of age, and another 19 years of age.

Table V represents an attempt to analyze the nature of our sampling of school population. It will be noticed that in the group of heart disease suspects there were more children between 10 and 15 years, and fewer between 6 and 9 years than in the standard population for these age periods. The question arises as to whether this concentration of cases in a certain age period may introduce an error in our estimate of the number of cases of organic heart disease occurring in the various age groups (Table IV).

TABLE V

COMPARISON OF AGE DISTRIBUTION OF 295 CARDIAC DISEASE SUSPECTS EXAMINED WITH AGE DISTRIBUTION OF TOTAL POPULATION IN SIMILAR AGE GROUPS

AGE DISTRIBUTION OF SAN FRANCISCO POPULATION BY HEMIDECADES U.S. CENSUS 1930		ESTIMATE OF SELECTIVE AGE GROUPS BY INTERPOLATION FROM U.S. CENSUS FIGURES		AGE DISTRIBUTION IN SERIES OF 295 CASES STUDIED IN THE SAN FRANCISCO GROUP	
5- 9 yr.	5.93%*	6- 9 yr.	29%†	6- 9 yr.	17.5%‡
10-14 yr.	5.68%	10-12 yr.	21%	10-12 yr.	28.8%
14-19 yr.	6.69%	13-15 yr.	23%	12-15 yr.	28.4%
		16-18 yr.	25%	16-18 yr.	25.0%
				19 yr.	0.3%

*Per cent of total population.
†Per cent of entire age group of 6 to 18 years.
‡Per cent of series of 295 cases studied.

Certain considerations lead to the belief that this disagreement in distribution of population does not influence materially the conclusions that may be drawn from the data presented in Table III. The incidence in our survey of organic heart disease occurring in children from the ages of 10 to 15 years agrees with estimates in other surveys. The common occurrence of "functional" murmurs between the ages of 6 and 9 years would account for the selection of a relatively large number of children of this age group as cardiac suspects, as was found in our study. Because organic heart disease is rare at this age, the

proportionately fewer cases found in this survey should not materially influence the total percentage of cases of organic heart disease in the entire age range studied.

It will be noted that four etiologic groups, other than those listed in Table II, have been added in Table IV, namely, doubtful rheumatic heart disease, doubtful congenital heart disease, potential rheumatic heart disease, and hypertension. Diagnoses were regarded as doubtful when the presence of a lesion could not be definitely established by means of the physical examination and history. Occasionally a case could not be classified with certainty as congenital or rheumatic, although it was recognized as one of organic heart disease. In such instances, the most likely diagnosis was made arbitrarily for the purpose of classification. Potential rheumatic heart disease was diagnosed when the history of rheumatic involvement was so recent that cardiac disease, although not sufficiently evident at the time of examination, possibly was present.

"Hypertension" was diagnosed when the systolic blood pressure was higher than 140 mm. Hg, but we realize that during the examination many of the children were apprehensive, and therefore it may be assumed that the initial readings in many instances were probably too high because of psychic as well as vascular instability. It is interesting that nearly 10 per cent of the children between the ages of 16 and 18 showed elevation of the systolic blood pressure, and that 64 per cent of them were boys. In this group, in contradistinction to true essential hypertension, the diastolic pressures were normal and the pulse pressures consequently high. Measurements such as 150/85 were common.

Little can be said of the frequency of "functional" murmurs in this particular group, for many children with such murmurs were not suspected of heart disease and therefore were not referred.

In the school survey (Table III), as at the Cardiac Diagnostic Center, the incidence of congenital heart disease was unusually high. It is significant that the figures show an approximately equal proportion of cases of rheumatic and congenital heart disease up to the age of 12 years, instead of the rising predominance of rheumatic heart disease between the ages of 10 to 12 years which has been observed by others (Tables IV and VI).

Table VI shows the proportionate incidence of rheumatic and congenital cardiac disease in cases of organic heart disease in various age groups.

Rheumatic heart disease was divided equally between the sexes (49 per cent boys, 51 per cent girls), which agrees with Christie's figures for northern California (48 per cent and 52 per cent, respectively).

Only 6, or less than 10 per cent, of the children with rheumatic heart disease or potential rheumatic heart disease had had their pri-

TABLE VI

PROPORTIONATE INCIDENCE, BY AGE GROUPS, OF RHEUMATIC AND CONGENITAL HEART DISEASE IN 79 CASES OF ORGANIC HEART DISEASE POSITIVELY DIAGNOSED IN 295 CARDIAC DISEASE SUSPECTS AMONG 18,607 SCHOOL CHILDREN

AGE GROUPS (INCLUSIVE)	RHEUMATIC		CONGENITAL		TOTAL NO. OF CASES
	NUMBER	PER CENT	NUMBER	PER CENT	
6- 9 yr.	6	54.5	5	45.5	11
10-12 yr.	12	54.5	10	45.5	22
13-15 yr.	18	65 +	10	35 −	28
16-18 yr.	12	68.5	5	31.5	17
19 yr.	1				1
Total	49	62	30	38	79

mary acute rheumatic attack before they came to San Francisco. This fact is important in comparing the incidence of rheumatic fever in this locality with that in other parts of the country. More instances might have been discovered if careful histories had been obtained from the parents in every case, but this was not always possible.

Table VII gives figures from a review of the literature dealing with the incidence of organic and rheumatic heart disease in school populations of the middle, western, and eastern United States, as well as Great Britain. The marked geographic differences in the incidence of organic and rheumatic heart disease in these localities may be noted. By statistical analyses of two series of cases, using in one instance an indirect and in the other a direct method of estimation, the low incidence for San Francisco school children is shown.

TABLE VII

INCIDENCE OF ORGANIC AND RHEUMATIC HEART DISEASE IN SCHOOL POPULATIONS OF THE UNITED STATES AND GREAT BRITAIN

LOCALE	NO. OF CHILDREN EXAMINED	ORGANIC HEART DISEASE PER 1,000	RHEUMATIC HEART DISEASE PER 1,000
San Francisco (Authors' Table III)	13,338*	3.7	2.20
San Francisco, 1931-1934 (Authors' Table II†)	86,082	3.7	1.55
Cincinnati, 1930[9]	6,960*	3.7	2.90‡
New York City, 1921[3]	44,000*	5.0	4.30
Boston, 1927[5]	119,337*	5.2	4.60
England and Wales[10]	598,167*	7.0	
Chicago, 1923[11]	158,826*	9.0	7.20‡
Philadelphia, 1929[4]	10,333*	9.1	8.20
New York, 1918-1922[12]	1,336,343*	13.9	
Gloucestershire, 1927-1930[13]	53,501*		1.03
Somerset, 1927-1930[13]	42,804*		2.17
Bristol, 1927-1930[13]	54,673		7.72
New Mexican Indians[14]	1,019		5.00
Northern Indians[14]	688		45.00
Philadelphia[7]	33,293	6.0	3.90
New Haven[15]	5,758		48.10

*Figures do not include a preschool group.

†Calculated from Table I on the basis that there were 321 cases of organic heart disease in a school population of 86,082 from 1931 to 1934, inclusive. It is assumed that patients examined at the Cardiac Center represent the heart disease suspects from the Well-Baby Conference plus 50 per cent of those examined at school.

‡Computed on a basis of 80 per cent of all cases of heart disease.

Figure 1 is an integral chart compiled from the data published by Geiger, Sampson, Miller, and Gray[2] on the incidence of heart disease throughout the city of San Francisco. It is presented to show that the figures for the first three hemidecades in the general population agree fairly well with the figures for the group studied in the schools. Because of the failure to divide the age group of 10 to 14 years, inclusive, the delayed rise in the incidence of rheumatic heart disease in this period is not as evident as from the figures shown in Table VI.

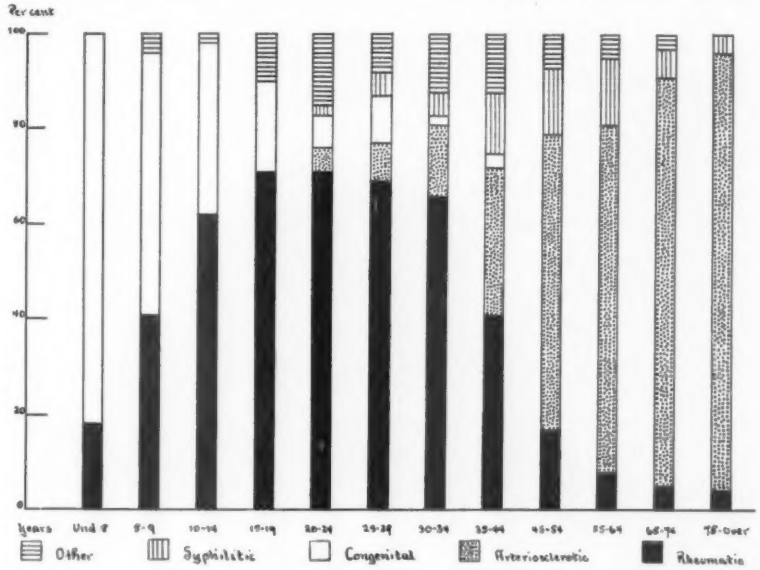

Fig. 1.—Comparative incidence of various types of heart disease in San Francisco by hemidecades and decades (From 1932 heart disease morbidity survey of Sampson, Geiger, Miller, and Gray[2]).

SUMMARY AND CONCLUSIONS

A study made at the San Francisco Cardiac Diagnostic Center in the years from 1931 to 1934 is reviewed. During this period, 1,197 children suspected of having heart disease were examined by the members of the staff of the Center. Three hundred twenty-one, or 26.8 per cent, were found to have organic heart disease. This represents an incidence of organic heart disease of 3.7 per 1,000 school children.

One of the authors (Christie) examined 485 of the 1,197 and found that 58 per cent of the children with organic heart disease had congenital heart disease. Similarly, in every study made on San Francisco school children, the percentage of cases of congenital heart disease in the organic heart disease group has been found to be extremely high, from which fact it has been concluded that the incidence of rheumatic heart disease must be correspondingly low. Judging from our study of patients referred to the Cardiac Diagnostic Center, the incidence of rheumatic heart disease in San Francisco school children

is approximately 1.5 per 1,000. This is probably not as accurate as the estimate from data obtained from a sample of the entire school population because we do not know exactly how many of the cardiac disease suspects in the entire school population were referred to the Cardiac Diagnostic Center. Likewise we believe that the average age of the patients studied at the Center was lower than the average age of all of the school children or of the sample taken from the schools.

A sample of 13,338 school children, selected because of uniformity of the population studied, contained 197 children suspected of having heart disease. In this group the incidence of organic heart disease per 1,000 population was 3.7; of rheumatic heart disease, 2.2; and of congenital heart disease, 1.4

From a larger group (18,607 children) of less carefully selected cases, data were obtained on the relative frequency of different types of heart disease in various age groups and in the two sexes.

The rates per 1,000 population for organic and rheumatic heart disease in San Francisco are compared to those of other school populations in the United States and Great Britain.

We are indebted to Dr. Paul S. Barrett, Director of the Bureau of Child Hygiene, to the Department of Field Nursing of the San Francisco Department of Public Health, and to the San Francisco Department of Education, for their helpful cooperation in assembling data for this study.

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SCLEROSING OF VARICOSE VEINS BY LIGATION AND ONE MASSIVE INJECTION OF SODIUM RICINOLEATE (SORICIN)*

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TO THE best of our knowledge, the earliest attempts to obliterate varicose veins were made by Provatz[1] in 1851. These attempts were somewhat successful, but there were many reactions and infections, and some fatalities. DeLore,[2] in 1894, first demonstrated the action of drugs which produce obliteration in the veins. Since the beginning of this method of treatment of varicose veins many types of solutions have been used with varying degrees of success.

The action of sclerosing agents has been carefully studied by animal experimentation and biopsy. These observations indicate that following the formation of an adherent fibrotic clot there is sufficient irritation to cause destruction of the intima of the vein. This is followed by the formation of a firm deposit of fibrin and blood platelets, resulting in the formation of a dense clot extending into the smaller vein which leads into the varicosity.

Figs. 1 to 4, photomicrographs of the cross section of the ear vein of a rabbit, show the effect of a 2 per cent solution of sodium ricinoleate (soricin) at intervals of fifteen minutes to twenty-four hours. It appears from the photomicrographs that the clotting of the blood is an immediate effect due to coagulation of the red cells and that it precedes the injurious effects on the lining of the vein. This clotting is a sudden event and does not follow the usual course of an ordinary, slowly developing ante-mortem thrombus. Within an hour after the injection of sodium ricinoleate, destruction and desquamation of the lining endothelium occur. Within twenty-four hours there is complete destruction of the intima of the vein, with some degenerative changes taking place in the surrounding tissue, probably due to an extension of the material out of the venules into the tissue spaces.

The chief danger encountered in this procedure is the possibility of deep vein sclerosis. This, we believe, is diminished by changing the posture of the patient immediately after the injection so that the foot becomes dependent. As soon as the wound is closed, the patient gets up and walks about. In our series there has been no obliteration of the deep veins. We attribute this to the fact that we make our patients become active at once and that we use a dilute solution. This is further diluted by the blood and cannot cause much damage to the intima of the vein thereafter.

*From the Peripheral Vascular Clinic of the North Side Unit, Youngstown Hospital Association.
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The sclerosing solution used in our work is a 2 per cent solution of sodium ricinoleate prepared in accordance with the directions of Rider.[3] The drug in this solution is approximately 98 per cent pure sodium

Fig. 1. Fig. 2.

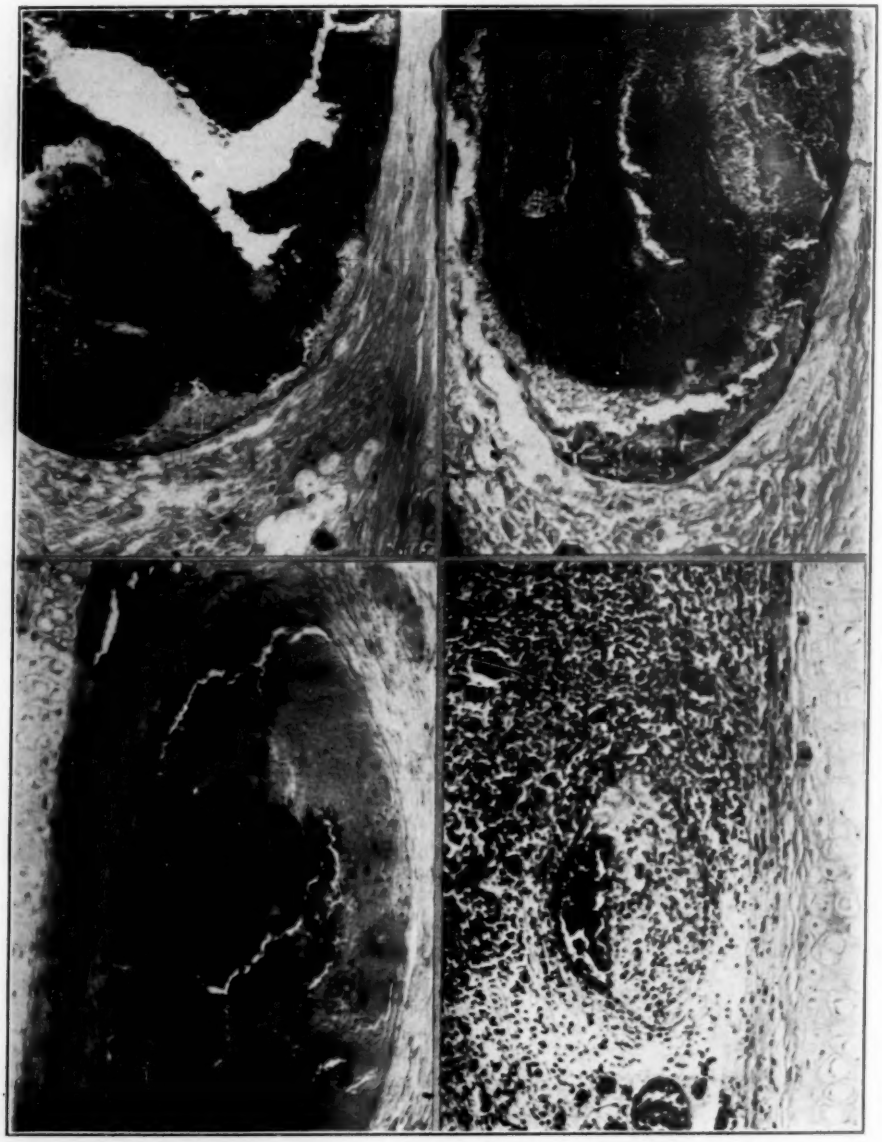

Fig. 3. Fig. 4.

Fig. 1.—Cross section of ear vein of rabbit fifteen minutes after injection of sodium ricinoleate.

Fig. 2.—Cross section of ear vein of rabbit one hour after injection of sodium ricinoleate.

Fig. 3.—Cross section of ear vein of rabbit six hours after injection of sodium ricinoleate.

Fig. 4.—Cross section of ear vein of rabbit twenty-four hours after injection of sodium ricinoleate.

ricinoleate, with small amounts of sodium oleate and sodium linoleate. We feel that one distinct advantage in the use of sodium ricinoleate is the fact that it is a known, stable compound, the composition of which can be controlled within very narrow limits. The 2 per cent solution has a pH which has been adjusted to 8.0.

Froehlich and Henrickson[4] report the use of 5 per cent sodium ricinoleate in the treatment of varicose veins in 300 patients. Their method was to give a preliminary injection of 1 c.c. into a small loop of the vein as a test to determine whether or not the patient was sensitive to sodium ricinoleate. If no sensitivity was evidenced, a 5 c.c. dose was used in a sufficient number of injections (averaging three to four in number) until all veins were sclerosed.

Postlethwaite[5] employed a 2 per cent solution of sodium ricinoleate, using only small amounts of the solution and making repeated injections until the entire vein became sclerosed.

Riddle[6] reported the use of 10 per cent sodium ricinoleate and found that it was effective even when 10 per cent sodium morrhuate or invert sugar had failed.

McPheeter[7] states that 5 per cent sodium ricinoleate is as good as sodium morrhuate but that it is a little stronger and gives more of a reaction. For this reason he is now using 2 per cent sodium ricinoleate in the larger veins and 0.5 per cent in the superficial vein ruptures.

Johnston[8] reports the use of a solution of 5 per cent sodium ricinoleate with ligation of the great saphenous vein and its branches at the femoral opening. He stresses the importance of ligating the branches to prevent recurrence and canalization. We believe that, if marked adhesions or lymphatic blockage are present, they contraindicate wide dissection to ligate the branches because the wound does not heal readily and marked seepage results. The destruction of the lymphatics by dissection results in the increased production of edema which persists for a long time and prevents further injection of the vein, should this be necessary. Johnston[8] also stresses the importance of testing the arterial circulation, with which we are in accord.

In the treatment of varicose veins, we have not been satisfied with the fractional injection of small quantities at the site of the varicosities. The disadvantages of this method of treatment consist of a period of disability and discomfort, lasting from four to seven days after each treatment, and a multiplicity of injections requiring from three to six months, accompanied by numerous periods of disability and discomfort scattered throughout the treatment. There is also to be considered the danger of the development of sloughs at the site of the injection.

Because of these disadvantages, we have adopted a somewhat different procedure in selected patients who have reacted satisfactorily to the Trendelenburg and Perthes tests, and have also had a thorough examina-

tion of the arterial system, including oscillometric readings, surface temperature readings, and Collens-Wilensky and Buerger tests.

In the Trendelenburg test the patient is placed in the decubitus position and the extremity is raised to empty the veins. A tourniquet is placed above the knee. The patient then stands. Quick filling of the veins from below upwards means that the communicating vein valves are incompetent and that there is overflow from the deep veins into the supercifial ones. When the tourniquet is released, if the saphenous vein fills rapidly from above as soon as the patient stands up, it indicates that the valves at the saphenofemoral junction are incompetent. The latter is a positive Trendelenburg test. A combination of the two is a Trendelenburg double test.

The Perthes test shows whether or not the femoral vein is patent. With the patient standing a tourniquet is placed above the knee just tight enough to cut off the superficial venous return. The patient then walks about the room several times. If the deep venous return is not adequate, pain will soon be experienced throughout the leg. If the deep veins are open, the dilated superficial veins tend to collapse and no pain will be produced. The collapse of the veins is due to the sucking out of the blood by muscular contraction. The blood is drawn through the communicating veins into the femoral system and then up through the femoral vein.

The Buerger test is performed by having the patient assume the supine position, elevate the legs, and flex and extend the ankle rapidly. The foot is observed for blanching, and any pain or cramp in the calf is noted.

The Collens-Wilensky test is performed as follows: The patient lies down and the foot is elevated until the superficial veins are collapsed. Then the foot is quickly lowered over the side of the bed and the time for filling of the superficial veins on the dorsum of the foot is noted. The normal filling time is from five to seven seconds.

COMPARISON OF METHODS OF TREATMENT

The treatment consisted in Group 1 of injections of various drugs and in Group 2 of ligation of the great saphenous vein and its branches, followed by multiple injections of 2 per cent sodium ricinoleate. Group 3 consisted of patients who were treated by ligation of the great saphenous vein and its branches, together with massive injections of a 2 per cent solution of sodium ricinoleate into the distal portion of the vein. This constitutes what we consider to be the most satisfactory method thus far described.

Group 1.—This group comprised 26 patients, all of whom showed a chemical thrombophlebitis at the site of injection. They were treated with multiple injections of various solutions: namely, sodium salicylate 30 per cent, averaging 207 c.c.—13 cases; sodium morrhuate, averaging 76 c.c.—9 cases; quinine hydrochloride and urethane, averaging 17 c.c.—4 cases. There were no ligations of the great saphenous vein in this group. Recurrence and canalization after two years occurred in 38½ per cent of the cases.

Group 2.—This group consisted of 78 patients who were treated by ligation of the great saphenous vein and its branches and multiple injections of 2 per cent sodium ricinoleate, averaging 48 c.c. There was no recurrence nor canalization after one and one-half years.

Group 3.—This group consisted of 31 patients who were treated by ligation of the great saphenous vein and its branches, when feasible, and injection of 2 per cent sodium ricinoleate, averaging 17 c.c. There was no recurrence or canalization after one year. In addition, iontophoresis of acetyl-beta-methylcholine chloride (mecholyl) and the application of the intermittent venous compression cuff (Collens-Wilensky) were used.

In Group 3, the new procedure was adopted only in selected cases, the criteria for the selection of which will follow.

The results are shown graphically in Charts 1, 2, and 3.

Group 1.—There were 9 ulcers (3 bilateral) in this group. The method of treatment employed did not lead to healing after one year's time. Relief of postinjection pain was never accomplished in less than

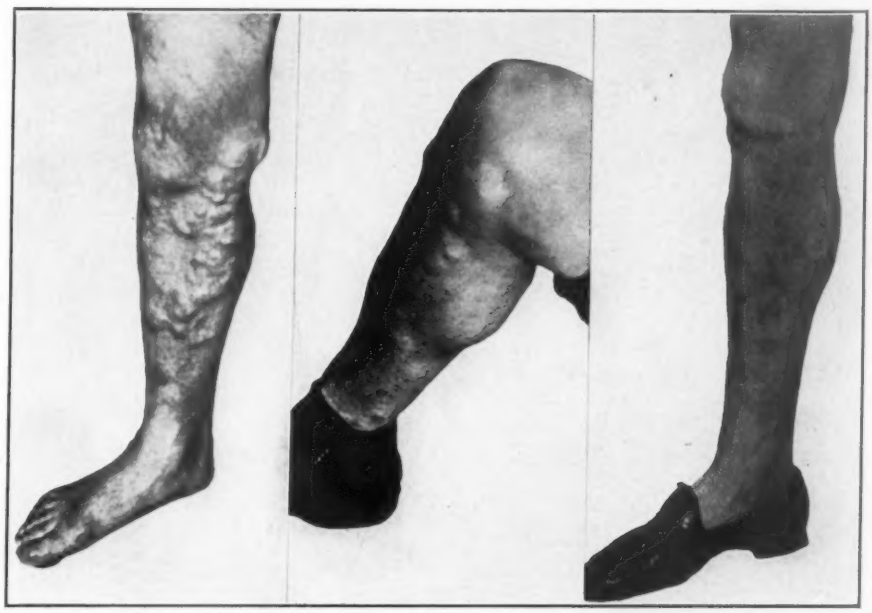

Fig. 5. Fig. 6. Fig. 7.

Fig. 5.—F. W., aged 52 years, a tailor. Varicose veins for fifteen years. Treated by ligation of great saphenous vein and injection of 27 c.c. of a 2 per cent solution of sodium ricinoleate.

Fig. 6.—F. W. Disability for one week. Marked induration and periphlebitis, chemical phlebitis. Mecholyl by iontophoresis, and Collens-Wilensky cuff, daily for one week, beginning forty-eight hours after injection and ligation.

Fig. 7.—F. W., six weeks later.

two weeks. In 11½ per cent of the cases disappearance of periphlebitis was evidenced within two weeks after completion of treatment.

Group 2.—There were 22 ulcers in this group in which healing occurred within twelve weeks (6 per cent of cases). Eight and one-half per cent of the patients were relieved of pain within one week. In 24 per cent of the cases the periphlebitis disappeared within one week.

Group 3.—There were 7 ulcers in this group, all of which were healed within nine weeks; 87 per cent of the patients were relieved of pain

within one week. In 84 per cent of the cases periphlebitis disappeared in less than one week, averaging four days.

In the treatment of superficial vein ruptures we have employed a 0.25 per cent to 0.5 per cent solution of sodium ricinoleate in doses of 0.25 to 0.5 c.c., and we have found that the sclerosing effects leave less discoloration than was experienced with any other solution. McPheeter[7] reports similar results. This good cosmetic effect is especially appreciated by the younger female patients.

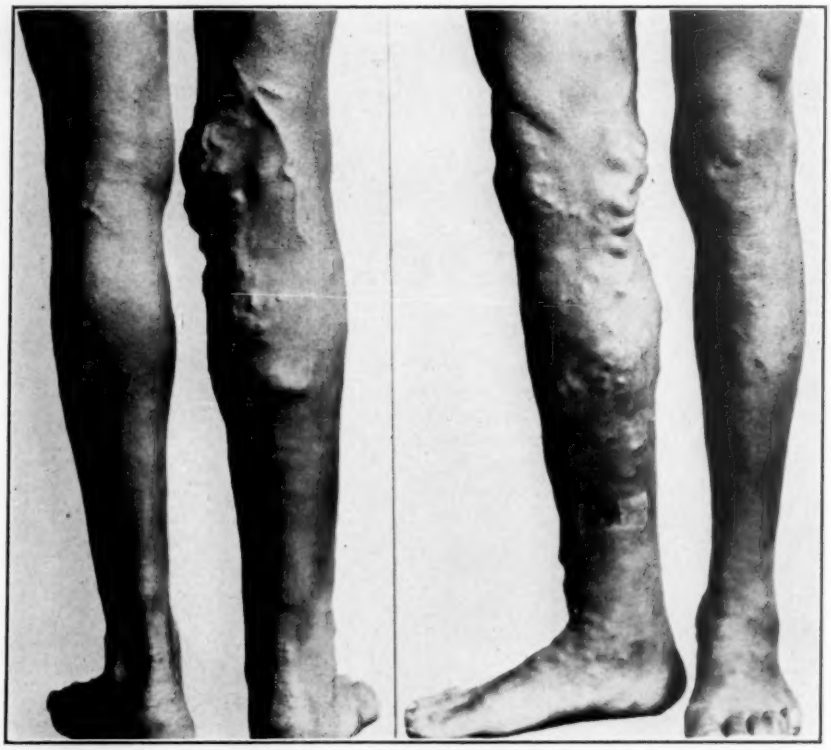

Fig. 8. Fig. 9.

Fig. 8.—C. R., aged 48 years, a laborer. Varicose veins for twelve years, ulceration for four years. Treated by ligation of great saphenous vein and injection of 22 c.c. of a 2 per cent solution of sodium ricinoleate. Mecholyl by iontophoresis, and Collens-Wilensky cuff, daily for two weeks, beginning forty-eight hours after injection and ligation. Ulcer healed. Disability lasted four days.

Fig. 9.—C. R., anterior view.

SELECTION OF CASES AND CONTRAINDICATIONS

Patients with varicosities which extended above the knee and those with varicose ulcers were selected for ligation. These patients were required to have adequate deep venous circulation as shown by the Perthes test.

In selecting the cases in Group 3, we excluded the aged (past 60 years), the very obese, high-strung nervous patients, and those with very chronic extensive, infected ulcers. All subjects were tested for the pres-

ence of latent infection by checking leucocyte counts and blood sedimentation time. Wassermann tests and complete urinalyses were made routinely. The presence of diabetes is a contraindication unless it is well under control. In patients with syphilis, antisyphilitic treatment is pushed energetically, and, when the ulcer shows healing, the treatment is conservative, namely, ligation and fractional injection.

This group does not include those patients who had, in addition to involvement of the great saphenous vein, varicosities of the lesser saphenous vein. These patients were placed in Group 2, inasmuch as they were subjected to ligation of the great saphenous vein and subsequent multiple injections.

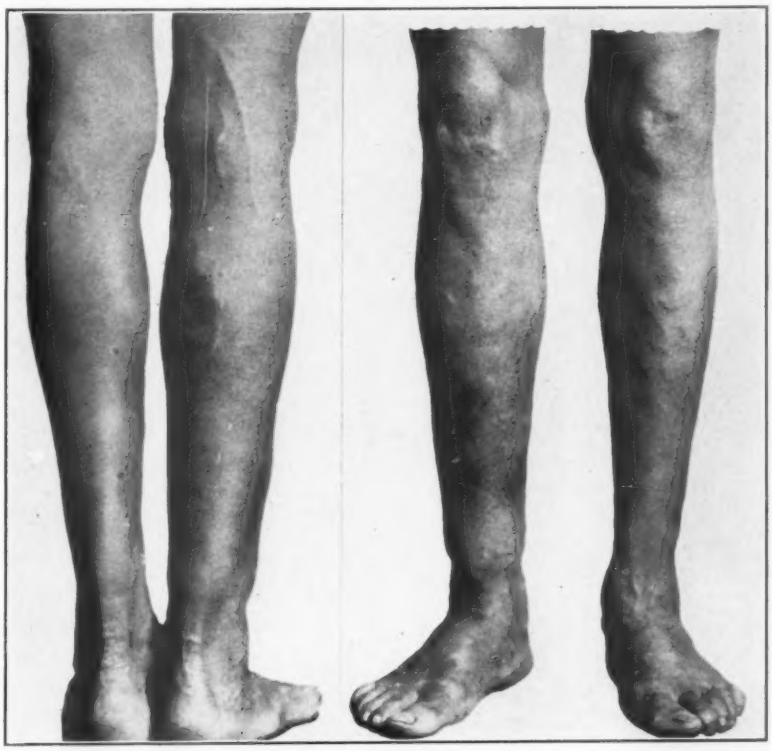

Fig. 10. Fig. 11.

Fig. 10.—C. R., posterior view two months later.
Fig. 11.—C. R., anterior view made at same time as Fig. 10.

TECHNIQUE

The technique was similar to that of Faxon[9] and Johnston,[8] namely, ligating and cutting the great saphenous vein near its entrance to the femoral and also ligating and cutting such branches as present themselves, avoiding undue dissection. The branches encountered are the superficial external pudendal, the superficial external epigastric, the superficial circumflex iliac, the internal superficial femoral, and the external superficial femoral veins.

A syringe filled with the desired amount of a 2 per cent solution of sodium ricinoleate is fitted with a fairly large bore needle (20 gauge), and the needle is inserted

distal to the first ligature. The suture placed around the distal portion of the vein is tied over the needle but is not tightened until after the solution is injected and the needle withdrawn. The amount of sodium ricinoleate used varied from 6 to

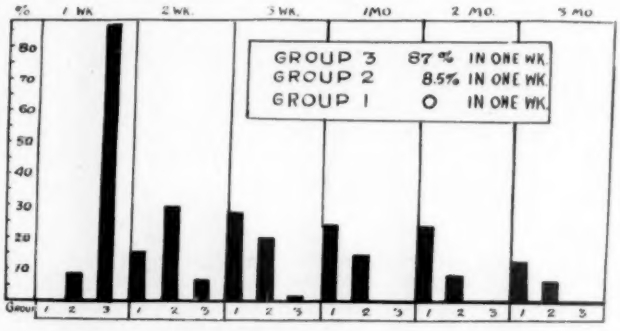

Chart 1.—Relief of pain.

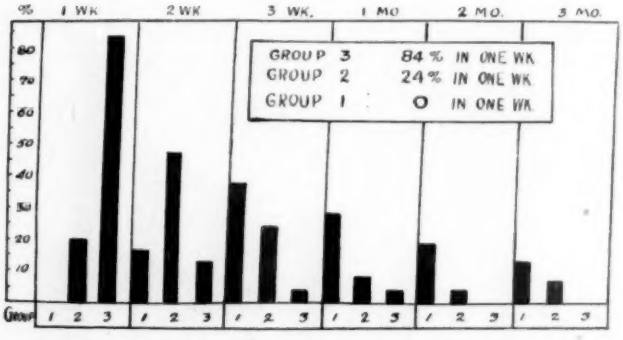

Chart 2.—Disappearance of periphlebitis.

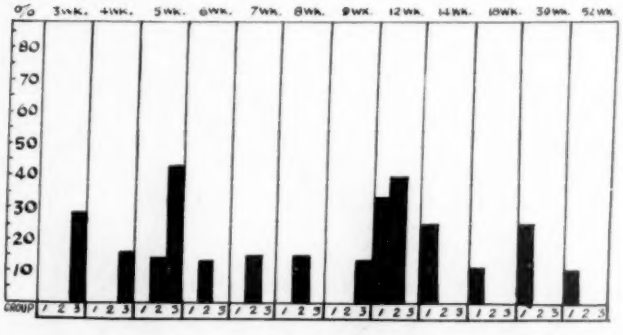

Chart 3.—Healing of ulcers.

Group 1, recurrence of varicose veins and canalization, 38.5 % (two years); Group 2, recurrence of varicose veins and canalization, 0 (one and one-half years); Group 3, recurrence of varicose veins and canalization, 0 (one year).

30 c.c. The vein is then ligated and severed between the distal and proximal ligatures. The proximal segment of the vein is doubly ligated as an added safeguard.

This method of treatment was employed in 31 patients and produced complete obliteration of all varicosities of the great saphenous tree.

AFTEREFFECTS AND REACTIONS

When the primary burning disappears, within a few minutes after injection, patients may get up. They usually complain of a "leaden," "heavy" feeling of the extremities. They claim that the legs feel "drawn" and "tight." Within twelve hours, a brawny induration of the entire extremity ensues. Within twenty-four hours, the skin over the vein becomes ecchymotic and the periphlebitis (due to penetration of the solution into the venules and tissue spaces) is quite painful. Within forty-eight hours some edema usually appears. Treatment of these two developments has consisted of application of the intermittent venous compression cuff (Collens and Wilensky[10]) and iontophoresis of acetyl-beta-methylcholine chloride (mecholyl).[11] As a rule, the pain and edema last from two to four days. The patient is usually not disabled and continues at his work.

AFTERTREATMENT

The day following injection, the patient returns to the clinic and receives a treatment by iontophoresis. This was instituted because it was noted that, when patients with severe periphlebitis and chemical thrombophlebitis were subjected to this treatment, following multiple injections (Group 1) without ligation, they responded with complete relief of pain, stiffness, and induration of the parts involved. On the next day, the intermittent venous compression cuff (Collens and Wilensky[10]) is applied to the thigh for a period of one hour or more depending upon the amount of discomfort produced and whether the edema increases. This treatment is given daily and is continued as long as there is periphlebitis and swelling.

The treatment of the ulcer also includes acetyl-beta-methylcholine chloride[11] by iontophoresis, the ulcer area being covered with vaseline gauze. After treatment, the ulcer is covered with a dressing of N:N-dichloroazodicarbonamidine (azochloramide) in oil. Activity is encouraged, and no elastic bandages are applied. In the last three cases, the azochloramide was made up into an ointment which contained 50,000 units of vitamin D to the ounce. This seemed less irritating and did not require vaseline protection.

DISCUSSION

After having tried various solutions for sclerosing varicose veins by injection, we resorted to a 1 to 5 per cent solution of sodium ricinoleate.

We have found that a 2 per cent solution of sodium ricinoleate is best suited for our purposes, inasmuch as adequate thrombosis is obtained without producing too severe a local reaction. In superficial vein ruptures 0.25 per cent to 0.5 per cent solutions were most satisfactory in our experience. Sclerosing effects were produced without undue discoloration.

The local reactive symptoms encountered, such as periphlebitis and painful thrombophlebitis, were treated at home by local applications of

aqua Hamamelidis compresses, with encouraging results. The induration about the veins was quickly relieved with acetyl-beta-methylcholine chloride[11] by iontophoresis. Paradoxical as it may seem, the edema produced was quickly reduced (in twenty-four to forty-eight hours) by the use of the intermittent venous compression cuff (Collens and Wilensky[10]) for two to six hours per treatment, forty-eight hours after ligation and injection. This is not begun sooner because the vein has been ligated, and there is danger of forcing off the ligatures. The result obtained may be explained by the facts that the venules were kept canalized and the edema was reduced by forcing an increased volume of blood through them.

Noting the good results obtained by the use of these agents in small veins, we injected the whole tree and treated the reactions in the same manner with surprising and satisfactory results.

SUMMARY

A method of treatment of varicose veins by injection of large amounts of 2 per cent sodium ricinoleate solution in the entire venous tree, together with ligation of the saphenous vein, is presented. The amount injected may vary from 6 to 30 c.c., depending upon the nature of the case. Cases should be carefully selected, excluding patients who have syphilis, diabetes, old, extensive, infected ulcers or who are extremely obese, or senile (past 60 years old). With this method, the length of treatment and time of disability have been considerably shortened, and the results appear more satisfactory than those following the use of other sclerosing solutions and other methods of procedure in the treatment of varicose veins.

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THE MONOCARDIOGRAPH*

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WILLEM EINTHOVEN, through his invention of the string galvanometer, provided us with an instrument of great sensitiveness and accuracy which made it possible to record and study the small electric currents generated by the hearts of animals and man. Physicians and physiologists, prominent among whom was Einthoven himself, soon laid the foundation of what has since been known as electrocardiography.

Electrocardiography was fortunate in its inception because it was established on a solid groundwork of well-developed physical and mathematical science. Although there was, and still is, some doubt as to the precise means by which the heart muscle generates an electric current, nevertheless, once such a current is generated, the mechanism of its spread and the recording of its characteristics are subject to precise and well-known physical laws. The use of the two arms and the left leg as contact or leading-off points provided constant and readily reproducible curves. These curves, as Einthoven showed, were readily susceptible to mathematical analysis.

This analysis is based on the fact that at any instant the differences of potential between the three leading-off points bear a simple relationship to one another, namely, that the difference of potential between the right arm and the left leg (known as Lead II) is equal to the sum of the potential difference between the right arm and the left arm (Lead I) and the potential difference between the left arm and the left leg (Lead III). The relationship can perhaps be better understood if we state it as follows: There are two ways of measuring the difference of potential between two points (right arm and left leg). We may either measure the difference of potential directly (Lead II), or we may select a third point (left arm) and measure the differences of potential between our original two points and this third point (Leads I and III), adding together these two differences. Obviously our answer will be the same whichever method we use.

Since the voltage of Lead II must at any instant be exactly equal to the sum of the voltages of Lead I and Lead III, Einthoven represented this fact graphically by means of a geometrical figure. He chose an equilateral triangle as the proper figure because the projections on the sides of an equilateral triangle of any line drawn within the triangle are so related that one projection is equal to the sum of the other two.†

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†This is, of course, a simplified and partial statement of the more general proposition that the projection of a line upon any side of an equilateral triangle equals the sum or difference of the projections of the same line upon the other two sides of the triangle.

Through the use of Einthoven's triangle it was possible to make a graphic representation of the voltage of the three leads of the electrocardiogram at any instant. By means of this triangle, mathematical and geometrical analysis of the electrocardiogram was facilitated. The two arms and the left leg are not placed at the apices of an equilateral triangle, and their actual spacing varies in different individuals. The use of an equilateral triangle does not presuppose that the leading-off points are equidistant from each other, but depends on the geometrical properties of such a triangle and its suitability for graphic representation of the electrocardiogram.

It would be desirable for an exact geometrical analysis of the electrocardiogram to know the exact distance of each electrode from the heart and from the other two electrodes, as well as the exact electrical characteristics and location of all the body tissues involved in conducting the electrical impulses from the heart to the electrodes. These various factors would have to be evaluated each time an electrocardiogram was taken. Obviously, even if we knew how to make all these evaluations, the enormous amount of work involved would be disproportionate to the results obtained. The use of the equilateral triangle for spatial analysis of the electrocardiogram involves an approximation which is unavoidable and one that varies with the electrocardiograms of different individuals. It has, however, the advantage of practicality and relative ease of application, and, provided the analyst bears in mind the necessary limitations of the method, Einthoven's triangle furnishes us with a valuable tool.

As a result of studying the mathematical and geometrical relationships previously discussed, the author devised and published in 1920[1] a method of analyzing the electrocardiogram. This method, based on Einthoven's triangle, consisted of measuring the voltage of the three standard leads at intervals of 0.01 second, and then plotting these voltages as a consecutive series of points on a polar curve. When these points were joined together as a smooth curve the result was a single curve embodying the three leads of the electrocardiogram. This single curve was called the monocardiogram.

The production of a monocardiogram from an ordinary electrocardiogram involved many hours of careful work. A photographic enlargement or camera lucida drawing of each lead was essential for accuracy. These enlargements were then measured at intervals of 0.01 second, and the measurements arranged, by trial and error, so that for every moment of the cardiac cycle Lead II equalled the sum of Lead I and Lead III. After mathematical computation the successive points of the monocardiogram were plotted on coordinate paper and connected with a fairly smooth curve.

The monocardiogram gave information of such value that the labor involved in producing this curve seemed justified, but, in addition to

the laboriousness of the process, the method described had several other drawbacks. In the first place, the use of the method required such a high degree of technical training and judgment that it could not readily be delegated to assistants, and therefore could not be made a routine procedure. In the second place, the final result was a curve drawn by hand on coordinate paper—a curve which might give the impression of being artificial, inaccurate, and not closely related to actual cardiac events. To many who did not concern themselves with technical details, the standard electrocardiogram seemed closer to reality than did the monocardiogram, which impressed them as a derived "imaginary" curve.

Both of these objections would be met and overcome if an instrument —the monocardiograph—could be devised to inscribe the monocardiogram automatically, without mathematical calculation and without the interposition of the human factor. This monocardiograph should be so designed that when connected to the two arms and the left leg it would produce a single polar curve instead of the three standard leads. This polar curve could be recorded photographically in a manner somewhat analogous to the recording of the electrocardiogram. For such an instrument a string galvanometer was not suitable. A combination of two mirror galvanometers might serve the purpose of combining two or more leads, but the available mirror galvanometers were slow and otherwise unsatisfactory for recording the electrical output of the heart. The cathode-ray oscillograph offered the best prospect of success in the construction of a monocardiograph.

The cathode-ray oscillograph operates by means of a beam of electrons which impinges on a fluorescent screen, making a small bright spot in much the same way that the narrow beam of flashlight is thrown against a wall. This beam of electrons can be deflected electrically so that the bright spot on the fluorescent screen moves and produces a curve which can be recorded photographically. The cathode-ray oscillograph has no appreciable lag, and will respond faithfully to vibrations much more rapid than those recorded in the electrocardiogram. It is not, however, as sensitive to small currents as is the string galvanometer, and therefore the electrical output of the heart must be amplified before it is led to the cathode-ray oscillograph.

In 1924 the author succeeded in producing an instrument which consisted essentially of two three-stage amplifiers actuating a cathode-ray oscillograph. When the two arms of a patient were connected to one amplifier and the left arm and left leg were connected to the other amplifier, the cathode-ray oscillograph produced a curve resembling the monocardiograms which had previously been drawn by hand. This curve varied in shape for different individuals, varied in direction when the heart was rotated by forced respiration, and varied in character for extrasystoles of different types. It had, however, serious drawbacks.

In the first place, it was not bright enough for good photographic recording, and the spot was too fuzzy and ill defined for accurate measurement. In the second place, because of the construction of the cathode-ray oscillograph, it was possible to use only two leads (namely, Leads I and III), and this introduced considerable error into the curves. Either a radical modification in the construction of the cathode-ray oscillograph would be necessary, or an entirely new instrument would have to be devised.

Nevertheless, this crude monocardiograph, consisting of two amplifiers and a cathode-ray oscillograph, was suitable for a demonstration of the validity of the method and of the objective existence of the monocardiogram. By means of this apparatus a demonstration of these points was made to a number of physicians, and, as a result of this demonstration, the Rockefeller Institute late in 1926 provided a grant for the construction of a better monocardiograph.

In 1926 the author began the construction of experimental galvanometers so designed that they would respond to three independent electrical currents. With the valuable assistance of J. F. Pattee, a galvanometer was finally designed and constructed which was capable of responding simultaneously to three separate electrical currents and had the required speed and accuracy for the recording of a monocardiogram. This galvanometer reflected a small, sharp, brilliant spot of light excellently suited for accurate photographic recording. It was actuated by three amplifiers, one corresponding to each lead of the electrocardiogram, and produced a curve indistinguishable from the mathematically derived monocardiogram. In 1931 this galvanometer with its amplifiers was demonstrated at the New York Academy of Medicine Graduate Fortnight. Since that time, the monocardiograph, of which this special galvanometer is the essential part, has been in almost constant use.

TECHNICAL DESCRIPTION

The monocardiograph consists of the following parts: (1) An *amplifier* which amplifies without appreciable distortion the currents obtained from the body, and actuates (2) a *galvanometer* which responds simultaneously to three currents corresponding to the three leads of the electrocardiogram. The deflections of this galvanometer are magnified by means of (3) an *optical system* and recorded upon (4) a *camera*. A detailed description of these parts follows.

1. The *amplifier* consists essentially of three similar three-stage amplifiers as illustrated in Fig. 1. To the three leading-off points of the body electrodes are applied as in ordinary electrocardiography. From these electrodes the voltages are brought to three similar wire-wound 300,000-ohm resistors which are matched within 1 per cent. By making these resistors equal, the symmetry of the system is preserved at this point. The same extremities of these resistors are connected to the grids of the first tubes of each amplifier. The other extremities are connected together through grid-bias cells which are grounded. This is the only point at which the input circuit is grounded. The patient is not connected to the ground or a shield at any point. This arrangement makes the amplifiers very sensitive to induction and necessitates careful shielding and elimination of stray fields.

The first two tubes of each amplifier are type 36 screen-grid radio tubes. They amplify the voltage about 2,500 times. The amplified voltage is fed to the third tube (171-A power tube). The third tube transforms the voltage into the desired

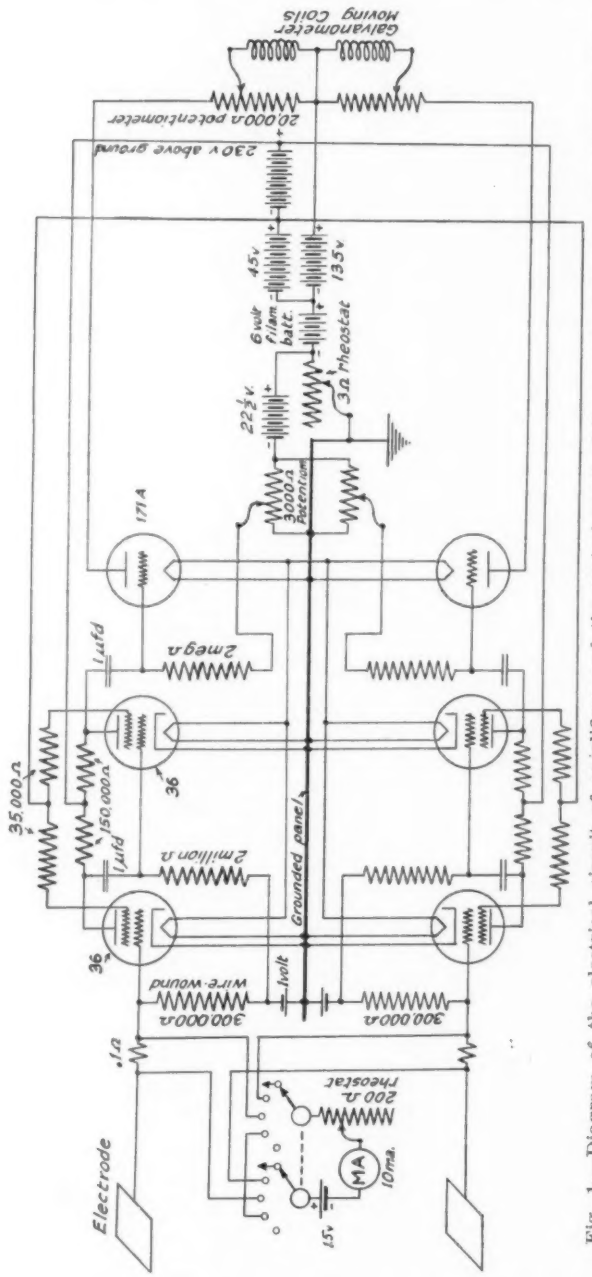

Fig. 1.—Diagram of the electrical circuit of amplifiers and the control panel of the monocardiograph. The diagram shows two three-stage amplifiers arranged symmetrically with respect to the grounded panel. In actual practice three such amplifiers are arranged symmetrically. The connections of the third amplifier, which is not shown in the drawing, are exactly the same as the connections of the two amplifiers shown. The three sets of amplifiers are all operated by the same batteries as shown in the illustration.

galvanometric value. The coupling circuits between the tubes (1-microfarad condensers and 2-megohm grid leaks) are designed to pass the slowest T-waves. The amplifiers can easily pass the fastest impulses the heart produces.

The negative potential on the grids of the three power tubes can be adjusted by three independent 3,000-ohm potentiometers. This changes the amount of steady current delivered by the tubes to the galvanometer without much changing the amplification. This operation is useful in adjusting the zero point of the galvanometer.

The gain from each amplifier can be attenuated at the galvanometer by three 20,000-ohm potentiometers. By adjusting these potentiometers the amount of amplification can be varied within wide limits (about 1,000 per cent), and the three amplifiers can be made exactly equal to each other.

The complete amplifier with its nine tubes, resistances, condensers, grid-bias cells, and control panel is mounted in a metal box which rests on an air cushion so that it is unaffected by external vibrations. The batteries for the filaments and the plates are located separately and connected to the amplifier by shielded cables.

For standardization, a separate box is provided, containing a dry cell, a rheostat to control current from the cell, a milliammeter to indicate that current, and a double-bank switch to switch that current to each of three equal resistors made of

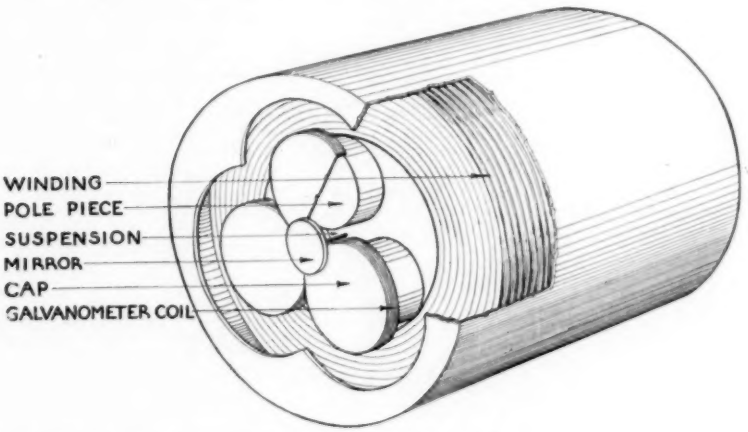

Fig. 2.—Diagrammatic representation of the special galvanometer used in the monocardiograph. The galvanometer *coils* are wound around the edges of the three *caps*, which are arranged in clover-leaf form. The curved *mirror* is rigidly attached to these three caps, which are fastened together and held in position by a *suspension*, which is merely a short straight wire. The caps are slightly larger than the *pole pieces* so that they can move without touching them. The field *winding* of the magnet is shown.

manganin alloy. These manganin resistors have a value (about 0.1 ohm) such that when the milliammeter reads 10 milliamperes there will be a voltage across them of 1 mv. (1 mv. = 1 R). The three resistors are connected in series with the patient leads as shown in the diagram (Fig. 1). When the current from the dry cell is adjusted by means of the rheostat to the standard value and the switch is turned, 1 mv. is applied to each of the amplifiers in succession. Thus each three-stage amplifier can be tested independently of the other two.

2. The *galvanometer* (Fig. 2) was designed especially for the monocardiograph. The moving part consists of a cluster of three movable coils, rigidly fastened together in one plane and pivoted universally at the center of gravity of the group. The framework of this system consists of three small, very light, duralumin caps, grouped like a clover leaf. The coils are wound around the edges of the caps. They consist of 1,500 turns of 0.001 inch insulated copper wire. The resistance of each coil is about 1,200 ohms. Very fine flexible leads are brought from these coils to fixed terminals.

The moving system is entirely supported by a very short bronze wire which is located at the center of gravity to minimize transfer of external vibrations. As each coil pulls or pushes in response to current fluctuations, the whole system tilts about its center of suspension. This it can do in any direction. The three coils are suspended in the air gap of a powerful electromagnet which has a three-knobbed pole piece, one knob projecting inside each cap. It is the reaction between the magnetic flux from this electromagnet, passing radially through the sides of the caps and the coils, and the current in the coils, which produces the motion. This same magnetic flux generates currents in the caps and coils when they are in motion which damp their tendency to vibrate and to overshoot. Air trapped inside the caps by the close fitting (but not touching) pole knobs also contributes to this damping. The result is that in spite of the weight and speed of the movable system it does not overshoot at all. A full deflection, approximately, can be obtained in 0.013 second. When used in connection with the amplifier and the optical system here described, this galvanometer can register a deflection of as much as 4 cm. per millivolt of current obtained from the patient. The whole galvanometer, which weighs about five pounds, is loosely hung in a rubber sling.

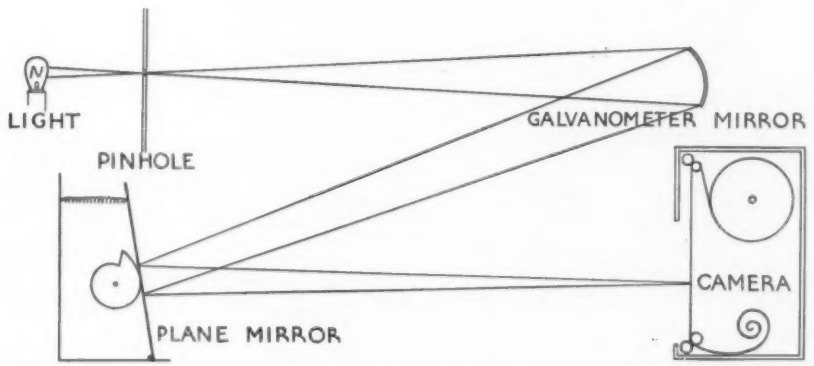

Fig. 3.—Diagrammatic scheme of the optical system of the monocardiograph. The *light* illuminates a *pinhole*, the image of which is reflected by the *galvanometer mirror* to a *plane mirror* and thence to the *camera*. The plane mirror is caused to oscillate by a cam in such a way that the image of the pinhole on the camera moves at the same speed as the sensitive paper.

3. The *optical system* (Fig. 3) is distinguished by its simplicity. No lenses are used, and only two reflecting surfaces are interposed between the lamp and the camera. The lamp, an ordinary concentrated filament lamp of 100-watt rating, illuminates a hole about 0.3 mm. in diameter, placed as near the lamp as possible. Through this tiny hole the light beam from a portion of the filament is directed upon the galvanometer mirror. This mirror, 5/16 inch in diameter and 1/32 inch thick, is concave, and aluminized on its front surface. It projects an image of the pinhole on a moving photosensitive surface. This projected image is about 0.5 mm. in diameter and is bright enough to give good photographic records. Greater brightness can be obtained by using an arc lamp, but this is not ordinarily necessary.

Before reaching the photographic paper (or film), the beam of light from the galvanometer is reflected from a plane mirror also aluminized on its front surface. This plane mirror is caused to oscillate by a very accurate spiral step cam. The cam, driven by the same shaft which drives the camera, swings the plane mirror through a small angle at a constant rate, so that the spot of light on the photographic paper moves with the paper, and at exactly the same rate, for about 1 cm. Then

a strong spring causes the mirror to snap back to its starting point in about 0.001 second, and the spot again follows the movement of the paper. Although the paper in the camera moves continuously, it is as if it were moved along by periodic jerks 1 cm. in length and lasting 0.001 sec., with a stationary period between jerks. The recording is done during the stationary period. In effect, the duration of the stationary periods is varied only by varying the speed of the motor.

4. The *camera* (Fig. 3) is of the continuous motion type. The sensitive paper, or film, is 6 cm. wide and 200 feet long. It passes over a series of rollers which move it at a uniform speed. During this motion it is exposed to the light beam described above and then is passed into a storage receptacle from which it is eventually removed for ordinary photographic development. The camera rollers are driven by a shaft actuated by a motor of adjustable speed. The speed of the motor is regulated by a rheostat.

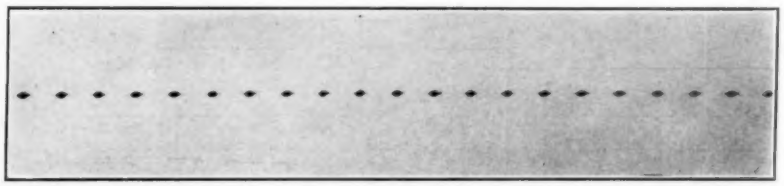

Fig. 4.—Record produced by monocardiograph when no patient is connected.

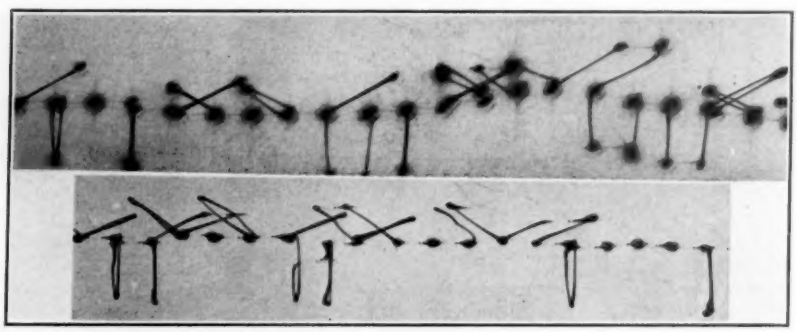

Fig. 5.—Record of standardization.

The operation of the monocardiograph is somewhat similar to the operation of an electrocardiograph. Electrodes are applied in the customary fashion to the two arms and the left leg. These electrodes are connected by a shielded cable to the amplifier. After turning on the amplifier, the lamp, and the galvanometer, the spot of light is centered on the camera by means of the potentiometers, and the amplification is adjusted to the desired degree. The standardization of each lead is tested and recorded on the first part of the film, after which the camera is allowed to run until a sufficient number of beats has been recorded.

Development and fixing of the photographic record follow.

SUMMARY

From the foregoing description it is evident that this instrument produces a curve by means described in 1920[1] as a "reversal of the process by which three leads are derived from one heart." The three leads are first amplified; they are then synthesized into one single curve; and finally this curve is recorded photographically.

MONOCARDIOGRAMS

For a clear understanding of the records produced by the monocardiograph it is advisable first to consider the record inscribed when the instrument is run without being connected to a patient. Fig. 4 shows such a record, a series of small sharp spots spaced about 1 cm. apart; it is to be read from left to right. This spacing is produced by the oscillating mirror previously described and is necessary for proper separation of consecutive waves. If a stationary spot of light were focused on the continuously moving sensitive paper, the result would be a continuous line, and any curves which might be produced would be distorted by the continuous movement of the tracing beam. The optical system used in the monocardiograph overcomes this difficulty by keeping the beam focused on one point of the moving paper for a definite period of time and then suddenly shifting the beam to a new center 1 cm. removed. Thus we obtain a series of frames similar to the separate frames of a motion-picture film.

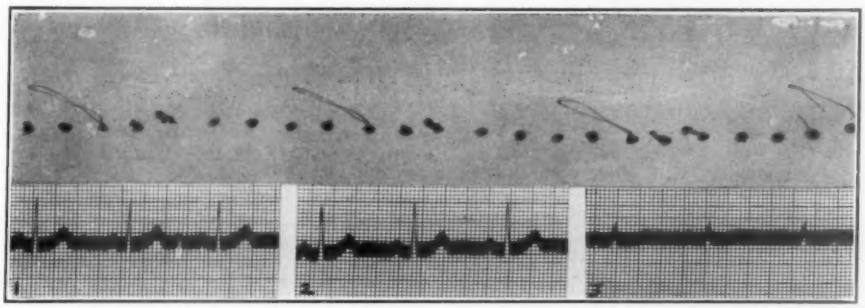

Fig. 6.—Normal monocardiogram. The electrocardiogram of the same patient is shown.

Fig. 5 shows a record of the standardization of the three leads, obtained by introducing a standardizing current of 1 mv. into each of the three sets of amplifiers. The galvanometer deflections occur in three directions separated by angles of 120 degrees, or, in other words, in a way which corresponds to the three sides of an equilateral triangle. It can be seen that the galvanometer does not overshoot and that it is deadbeat.

Fig. 6 illustrates the succession of events when a patient with a fairly normal heart is connected. This record, reading from left to right, consists of a succession of small spots, or frames, and in addition there occurs at regular intervals a series of curves or waves, as follows:

(1) An auricular wave which corresponds to the P-wave of the electrocardiogram. This wave is generally small and ill-defined with the amplification here used. In records of patients whose electrocardiograms show large P-waves, the monocardiogram shows distinct auricular waves.

(2) A large, smooth curve which represents the major electrical activity of the ventricles, and corresponds to the QRS-wave of the electrocardiogram.

(3) A rather small wave which represents the terminal ventricular activity, and corresponds to the T-wave of the electrocardiogram.

When the patient exhibits muscle tremor or slight movements of the large muscles, the smaller waves of the monocardiogram are obscured, and only the main ventricular deflection is recorded clearly. Because of its magnitude and the ease with which it is recorded, this main complex is most accessible for preliminary study. Most of our observations will center around this part of the monocardiogram.

The relationship between the main deflection in the monocardiogram and in the three leads of the standard electrocardiogram is illustrated in Fig. 7. This figure shows the monocardiograms of two patients, each surrounded by the three leads of the corresponding electrocardiogram, properly arranged on the sides of Einthoven's triangle. The first mono-

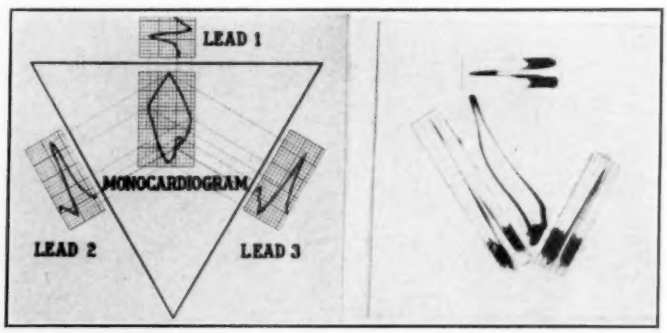

Fig. 7.—Relationship of monocardiogram and electrocardiogram shown graphically by means of Einthoven's triangle.

cardiogram was not recorded instrumentally, but was derived mathematically and geometrically from three simultaneous leads of an electrocardiogram originally published by Einthoven.[2] The second monocardiogram was recorded directly by connecting the patient to the monocardiograph. It can be seen that in each instance the central curve or monocardiogram represents a combination or fusion of the three leads into a single polar curve, or that, conversely, the three standard leads represent projections of the monocardiogram upon the sides of Einthoven's triangle. Every monocardiogram can be similarly arranged inside Einthoven's triangle with the leads of the corresponding electrocardiogram arranged on the three sides of the triangle.

It is to be noted that the monocardiogram does not have time lines such as are customarily recorded on the standard electrocardiogram. The monocardiogram, being a polar curve, uses both the horizontal and vertical dimensions to indicate voltage. Because of this it has a directional significance which is obscured in the ordinary electrocardiogram,

in which the horizontal axis is devoted to time indication and only the vertical axis can indicate voltage. The ordinary electrocardiogram is especially well-suited to the recording of cardiac arrhythmias and curves in which measurement of the time element is important. The monocardiogram, on the other hand, is not well-suited for time measurements, but is especially adapted to measurements of spatial relations, such as changes in the cardiac axis, location of site of origin of extrasystoles, localization of myocardial impairment, etc. This will become clearer upon study of the curves which follow.

Nevertheless, there are in the monocardiogram certain indications of time relationships which will repay study. With the camera running at any constant speed the spacing of the various waves will give a fair idea of their temporal sequence. In studying a single wave one should remember that the darker or heavier parts of the curve represent the slower movements of the galvanometer, and that, when the galvanometer

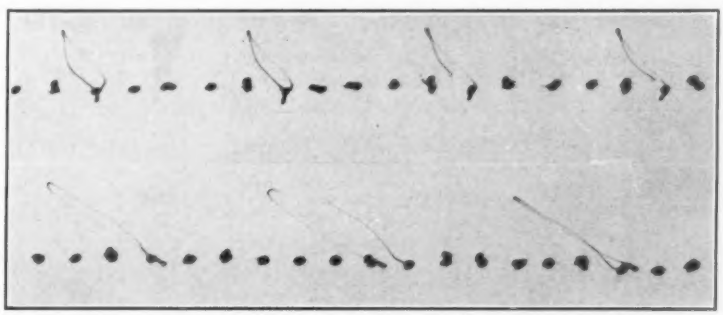

Fig. 8.—Normal monocardiograms.

moves more rapidly, the resulting line is thinner and fainter. But there is one temporal relationship not recorded by the electrocardiograph which is brought out clearly in the monocardiogram. This is indicated by the direction in which the main deflection is traced. The main deflection, being in most cases a closed curve, might obviously be traced in one of two ways, namely, either clockwise or counterclockwise. Either method of tracing would produce the same curve, for the beginning and the end of the curve are in the same spot. It will be noted that in some of the records the tracing beam has shifted to a new center or frame when the curve has been only partly traced. This produces a peculiar effect due to the fact that part of the curve is in one frame and the remainder in the following frame. Obviously the part of the curve which is traced first appears in the first frame and the later part of the curve appears in the later frame. This division of the curve into two successive parts gives information about which part of the curve is traced first, and thus shows whether the curve was traced in a clockwise or counterclockwise direction.

Not all curves can be so interpreted. Some curves of peculiar shape are partly clockwise and partly counterclockwise. It is difficult to follow the direction of S-shaped curves and very narrow loops, but the clockwise or counterclockwise course of the vast majority of monocardiograms can be traced very easily.

The monocardiograms of two patients whose electrocardiograms are fairly normal are reproduced in Fig. 8. Each record shows a main deflection which has been recorded in two frames, and it can be seen that the curves are traced in a clockwise direction. Both records show main

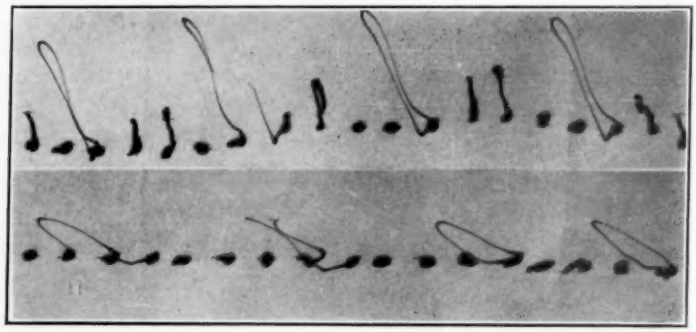

Fig. 9.—Upper curve shows prominent T-wave. Lower curve shows counterclockwise direction of the main deflection.

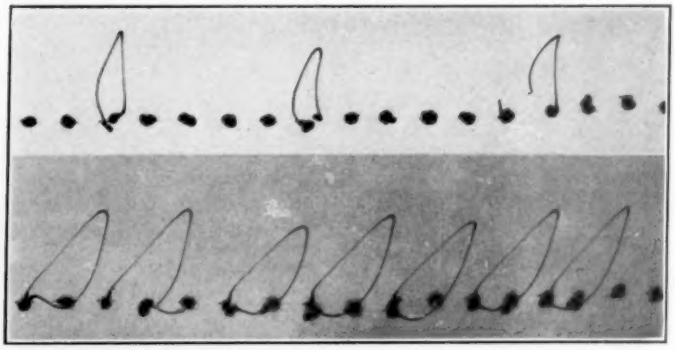

Fig. 10.—Right ventricular predominance.

deflections which are directed upward and to the left of the zero point or central spot, thus corresponding to a main deflection which is upright in Leads I and II of the electrocardiogram. The main deflection in the monocardiogram is a fairly smooth, rounded curve, without sharp breaks or irregularities. The standardization of these and succeeding curves is roughly twice normal, i.e., 1 mv. produces a deflection of about 2 cm. In spite of this, the P- and T-deflections are small.

Fig. 9 shows the monocardiogram of a patient with prominent T-waves. The second monocardiogram is of interest because of the fact that the main deflection is traced in a counterclockwise direction.

Fig. 10 shows the monocardiogram of a patient in whose electrocardiogram the R-wave was very low in Lead I and that of a patient with frank right ventricular predominance (this patient also has auricular fibrillation). In right ventricular predominance the main deflection of the monocardiogram is directed upward and to the right, corresponding to an inversion of the main deflection in Lead I of the electrocardiogram.

With left ventricular predominance the main deflection of the monocardiogram is directed to the left and downward, corresponding to inversion of the main deflection in Lead III of the electrocardiogram. Fig. 11 illustrates this, as well as the fact that most monocardiograms showing left ventricular predominance are traced counterclockwise, in contrast to the clockwise direction of most curves with no predominance or right predominance.

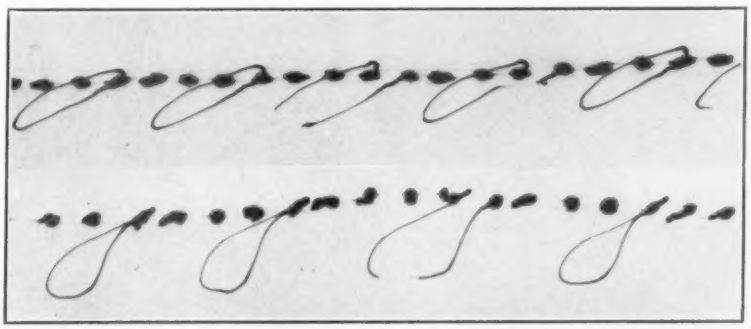

Fig. 11.—Left ventricular predominance.

Figs. 8, 9, 10, and 11, when examined with respect to the direction in which the curve points, indicate the cause for inversions of the main deflection in the electrocardiogram. When the monocardiogram points upward and to the observer's right, as in Fig. 10, it is evident that a projection of this curve upon Einthoven's triangle will produce an inverted main deflection in Lead I, as in right ventricular predominance. When the monocardiogram points upward and to the observer's left, as in Fig. 9, Leads I and II of the electrocardiogram will be upright, and the main deflection in Lead III may vary from the upright position to slight inversion. When the monocardiogram points downward and to the observer's left, as in Fig. 11, the electrocardiogram must show definite inversion of the main deflection in Lead III, as in left ventricular predominance.

The direction in which the monocardiogram points can be changed by forced respiration while a record is being taken, and this respiratory change affords a method of observing and measuring the respiratory mobility of the heart.

Fig. 12 shows two monocardiograms in which the main deflection does not fall into the simple classification previously given. The electrocardiograms of these patients are likewise anomalous.

Thus far, all of the monocardiograms shown have had main deflections of fairly smooth contour. The smooth contour suggests a smooth or regular spreading of the excitation wave through the ventricles such as normally occurs with an intact conduction system. Impairment of the intraventricular conduction system or interference with the normal mechanism of ventricular excitation may be expected to produce definite changes in the monocardiogram. On a priori grounds we would

Fig. 12.—Mixed predominance.

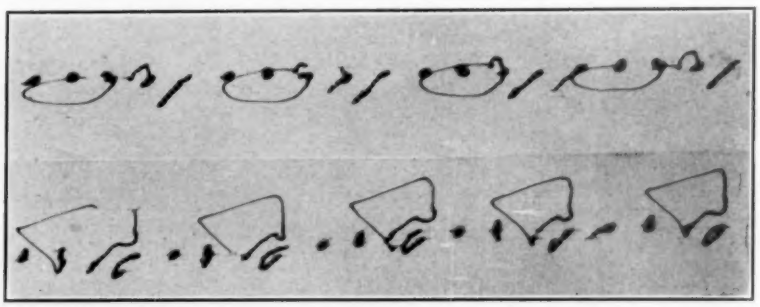

Fig. 13.—Intraventricular conduction defects.

assume that, when the spread of intraventricular excitation is seriously impaired, the main deflection of the monocardiogram will show evidences of abnormality, such as peculiar or irregular contours. In actual records such evidences of abnormality are commonly encountered in the monocardiograms of patients with intraventricular conduction defects. Not only do the main deflections in the monocardiogram assume peculiar and bizarre shapes, but the normally smooth curve is often replaced by one of irregular, notched or eroded contour. The curves which follow illustrate conditions in which there is impairment or disturbance in the normal mechanism of ventricular excitation.

Fig. 13 illustrates this irregularity of the main deflection. The first curve shows a main deflection which is fairly normal in contour through-

out most of its course, but is suddenly interrupted in its terminal portion by an irregular arc which is not a smooth continuation of the previous curve. This first curve also shows left ventricular predominance and a prominent T-deflection which is inverted in Leads II and III of the electrocardiogram. The second curve shows a main deflection, the terminal third of which is distinctly irregular. Here again the T-waves are abnormal.

The great variety of curves which correspond to intraventricular conduction defects is illustrated in Fig. 14. Here it is evident that those curves which in the electrocardiogram are ascribed to "arborization block" present in the monocardiogram a variety of abnormalities which will provide a separate field for study, classification, and interpretation.

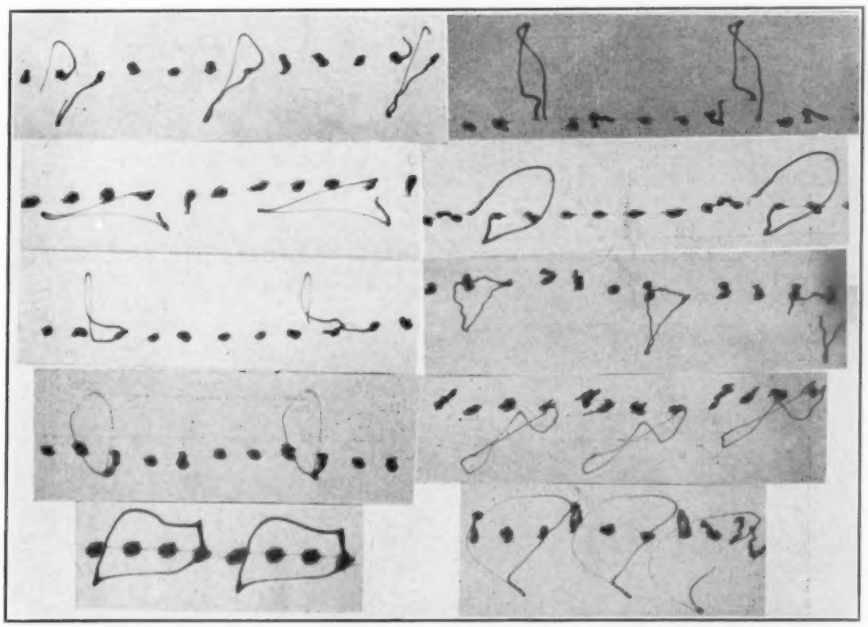

Fig. 14.—Curves showing a variety of intraventricular conduction defects.

Bundle branch block produces characteristic changes in the monocardiogram. In Fig. 15A* the main deflection is directed downward and to the observer's left, which direction is the result of left bundle branch block, and in Fig. 15B the main deflection is directed upward and to the right, indicating right bundle branch block. The patient whose monocardiogram is reproduced in Fig. 15B had a congenital septal defect. Roentgenkymograms made by Dr. Seth Hirsch gave evidence of a definite delay in the contraction of the right ventricle.

Acute coronary artery disease, as opposed to chronic myocardial damage, is known to produce gross changes in the R-T transition and in the T-waves of the electrocardiogram. The monocardiogram shows

*The courtesy of Dr. Ernst P. Boas made it possible to obtain this record.

these changes in a characteristic way. Fig. 13 shows abnormal T-waves. In normal monocardiograms the T-deflection points upward and to the observer's left, as does the main deflection. A T-deflection which points to the right indicates an inverted T-wave in Lead I of the electrocardiogram. A T-deflection which points horizontally to the left, or downward, corresponds to inversion in Leads II and III of the electrocardiogram.

In Fig. 16A, from a case of coronary occlusion, the T-wave points to the observer's right. The main deflection fails to return to the central (isoelectric) spot, indicating an abnormal take-off of the T-wave. Fig.

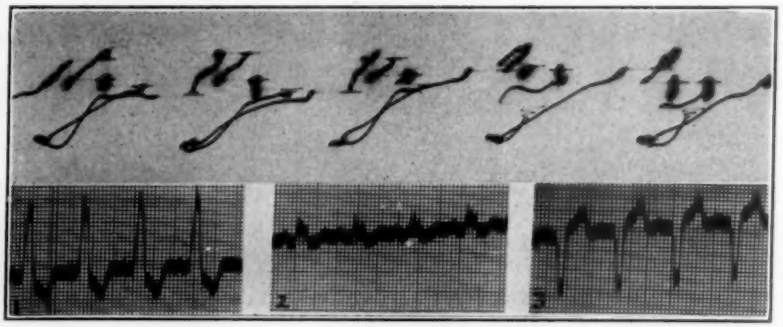

Fig. 15A.—Left bundle branch block.

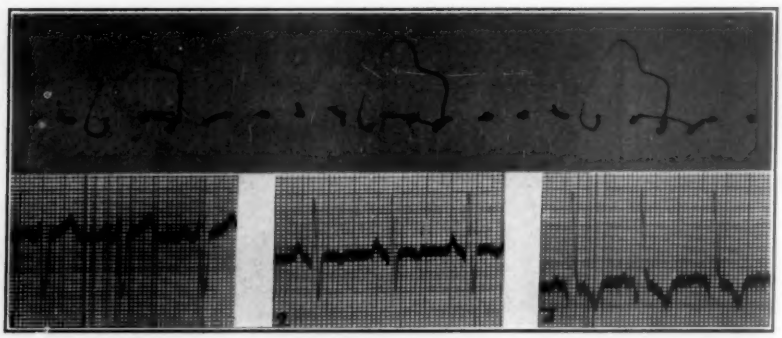

Fig. 15B.—Right bundle branch block.

16B shows a T-wave which is directed downward and to the left, indicating inversion of this deflection in Leads II and III. In both of these curves the main deflections show evidences of abnormality.

Extrasystoles provide a fertile field for monocardiographic study. The direction in which the extrasystole points gives evidence of its origin; one should always bear in mind that Einthoven's triangle is so drawn that the right side is to the observer's left, and vice versa. In Fig. 17 the first curve illustrates an extrasystole which apparently arises in the region of the right apex. The second curve shows an extrasystole which seems to arise at the left base. Fig. 18 illustrates the bizarre forms which extrasystoles sometimes assume.

In the following discussion of the significance and uses of the monocardiogram, the author has made use of several hundred monocardiograms taken during the past six years. The curves reproduced in this

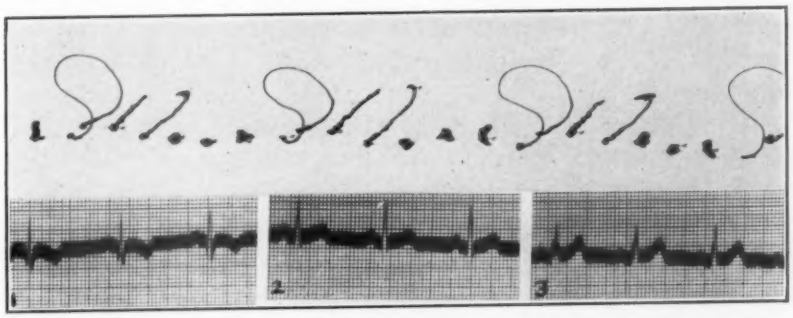

Fig. 16A.—Abnormal T-wave of the type generally associated with anterior coronary closure.

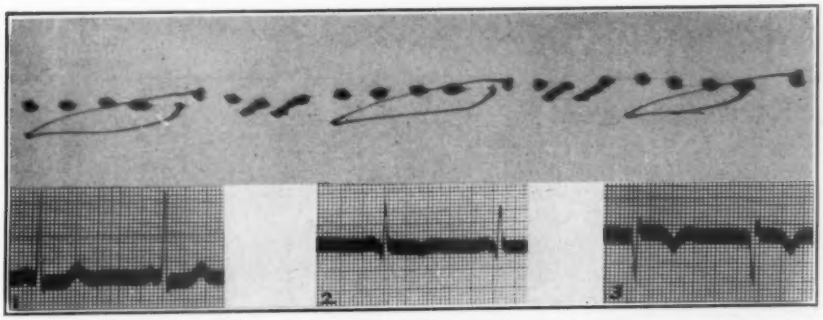

Fig. 16B.—Abnormal T-wave of the type generally associated with posterior coronary closure.

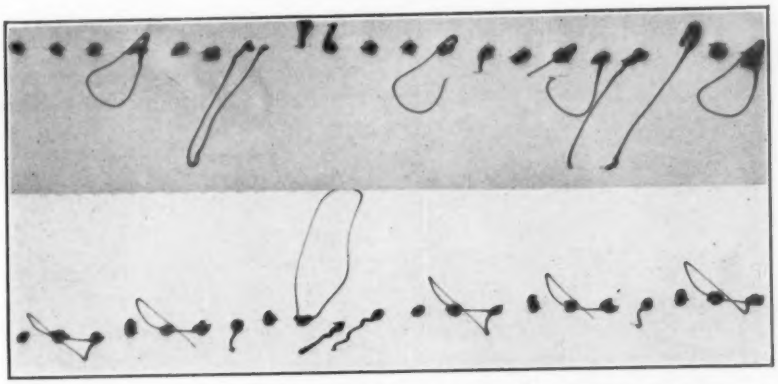

Fig. 17.—Ventricular extrasystoles interrupting sinus rhythm.

article, although limited in number, will serve to illustrate many of the points here considered.

Very early in the work evidence began to accumulate as to the directional significance of the monocardiogram. About 1926, when the monocardiograph in its crude form consisted of a cathode-ray oscillograph

with two amplifiers but with no permanent recording device, an opportunity was presented for testing the directional significance of the curves. A patient who had had part of the left chest wall removed some years previously was the subject. In this patient the precordium was covered only by fibrous tissue and skin, so that it was easy to produce extrasystoles by tapping lightly over the precordium. It was not possible to say with certainty which ventricle was being stimulated, but one could be reasonably certain whether he was tapping near the base of the heart or near the apex. The monocardiograms of these extrasystoles were upright when the base of the heart was tapped, inverted when the apex was tapped, and intermediate in form for intermediate points. Even before this it had become evident from direct observation that hearts of different shapes and sizes gave quite different curves and that right and left ventricular predominance produced characteristic changes in the direction of the main deflection. Forced respiration fre-

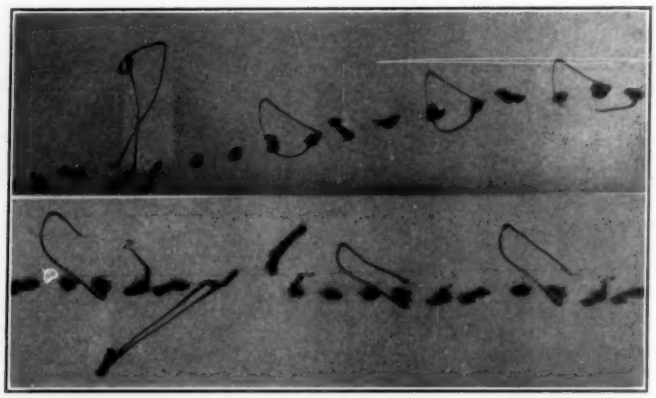

Fig. 18.—Bizarre type of ventricular extrasystoles.

quently produced rotation of the monocardiogram corresponding to the known direction of anatomical rotation.

These observations have been confirmed and extended by a study of the recorded curves, so that it is now possible to say with reasonable assurance that the monocardiogram, as recorded, has a directional significance which is only obscurely revealed by the electrocardiogram. The monocardiogram has sacrificed the time axis of the electrocardiogram and is therefore unable to delineate the arrhythmias, but in doing this it has gained a second space axis, so that it is able to record spatial and directional relations which have hitherto been obscure. In the curves which show these spatial and directional relations, extrasystoles stand out as prominent and relatively simple examples. The monocardiogram, as recorded, gives valuable evidence as to the site of origin of ventricular extrasystoles, and a classification of such extrasystoles according to the direction and shape of their monocardiograms should be of value.

There are many less spectacular spatial and directional features of the monocardiogram which should reward the investigator. The significance of clockwise or counterclockwise tracing of the various waves is obscure, but may be significant, and will probably repay careful study. Ventricular predominance produces obvious changes in the monocardiogram, and, if great accuracy is desired, the direction in which the monocardiogram points can be indicated by degrees. Right and left bundle branch block produce characteristic monocardiograms in which the activity of the intact ventricle obviously precedes that of the other.

Myocardial and coronary disease are interesting fields for monocardiographic study. As we have seen, monocardiograms of "arborization block" reveal abnormalities of certain parts of the main deflection. A study of these abnormalities may give valuable information, and the location of the lesion in coronary artery disease may be ascertained with considerable precision. By taking monocardiograms from three points in a frontal plane, instead of the usual sagittal plane, further information about anterior and posterior lesions may become available.

Auricular flutter and fibrillation suggest further uses for the monocardiogram. With increased amplification and suitable patients, it is not unreasonable to expect that we may be able to investigate the circus movement of flutter and possibly discover its location. The irregular circus movement of auricular fibrillation may yield records of interest and value.

SUMMARY

After a discussion of the principles underlying the monocardiograph, and a brief history of the evolution of this instrument, a detailed description of the instrument follows. The nature of the curves obtained by means of the monocardiograph is explained, and examples are given of monocardiograms characteristic of normal hearts and those which show ventricular predominance, "arborization block," bundle branch block, coronary artery disease, and extrasystoles.

The author wishes to express his thanks and appreciation to John F. Pattee for his indispensable assistance in designing and constructing many of the parts of the monocardiograph, and to Dorothy Rolph for her drawings.

The construction of the monocardiograph was aided by a grant from the Rockefeller Institute, to which the author wishes to express his appreciation.

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THE PRECORDIAL ELECTROCARDIOGRAM IN MYOCARDIAL INFARCTION*†‡

I. Observations on Cases With Infarction Principally of the Anterior Wall of the Left Ventricle and Adjacent Septum

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New York, N. Y.

THIS paper is the first of a series dealing with the potential variations of six precordial points, and of the right arm, left arm, and left leg, in cases of myocardial infarction. Our work was an outgrowth of the detailed experiments of Wilson, Hill, and Johnston,[1] who have demonstrated[1, 2] that the chief difference between precordial and direct leads is quantitative and that human precordial electrocardiograms are comparable to experimental direct leads in dogs. Between the two, however, there are several important differences which will be pointed out later. In this work we have adopted the method introduced by Wilson and his associates[4] and used by Wilson[3] in his study of 60 cases of myocardial infarction.

Our series comprises 127 cases of myocardial infarction. Of the 22 patients known to have died, 17 were subjected to post-mortem examination. Because an analysis of the necropsy observations is necessary for a proper understanding of the many cardiac factors which influence the precordial electrocardiogram, these observations have been divided into several groups. The first group, with which this paper is concerned, includes 4 cases of infarction principally of the anterior wall of the left ventricle, in 3 of which the anterior portion of the interventricular septum was also involved.

METHODS

In each case the standard leads were recorded first. The potential variations of the right arm (V_R), the left arm (V_L), the left leg (V_F), and of six precordial points were then obtained by pairing an exploring electrode with a central terminal connected to the right arm, the left arm, and the left leg, through resistances of 5,000 ohms each. This method has been shown to yield curves which represent the potential variations of the exploring electrode; the central terminal remains at zero potential throughout the cardiac cycle.[4] The following precordial points were explored: the fifth rib at the right sternal edge (V_1); the fifth rib at the left sternal

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edge (V_2); the fifth intercostal space in the left parasternal line (V_3); the fifth intercostal space in the left midclavicular line (V_4); the sixth rib in the left anterior axillary line (V_5); and the tip of the ensiform cartilage (V_E). In taking the extremity and precordial potentials the connections to the galvanometer were so arranged that a downward movement in the finished record represented positivity of the exploring electrode.*

The galvanometer was a Hindle No. 2, made by the Cambridge Instrument Co., and the string resistance was 4,000 ohms. The string was connected to the balanced plate circuit of a single-stage vacuum tube amplifier. Standard leads and extremity potentials (V_R, V_L, V_F) were taken at normal, precordial potentials at half-normal (1 cm. = 2 mv.), sensitivity of the string. The exploring electrode was a piece of sponge moistened with saturated salt solution, which made contact in the lower end of an ordinary glass test tube with a German silver plate.

At necropsy, the heart was opened in the usual way by following the path of the circulation. Macroscopic observations having been made and recorded, the specimen was fixed in Kaiserling I solution for a variable period, usually longer than twenty-four hours. Photographs were taken when indicated, and the heart was then sutured together again. At this stage the coronary arteries were examined by making transverse incisions ½ cm. apart down to the smallest visible branches. In every specimen an attempt was made to identify and study the following vessels: the left coronary artery and its branches, i.e., ramus descendens anterior and its accessory branches, ramus circumflexus, rami marginis obtusae, rami ventriculi sinistri posteriores, and the ramus descendens posterior (when present); the right circumflex coronary artery and its branches, i.e., rami anteriores, ramus lateralis (margo acutis), ramus ventriculi dextri posterior, ramus descendens posterior, and the rami ventriculi sinistri posteriores. Needless to say, the course, particularly of the descending rami, and the number and size of rami of the main branches, showed some variations. The coronary arterial system of each heart was drawn diagrammatically to scale with the lesions observed represented in code (Fig. 3 and legend). In every instance arterial abnormalities seen with the naked eye were checked microscopically. Even if no obvious change was encountered, sections were taken for microscopic study from the left and right coronary arteries, the ramus circumflexus, the ramus descendens anterior, and the ramus descendens posterior. Macroscopic abnormalities noted in the coronary veins were similarly dealt with.

The sutured heart was then placed in a rotary slicing machine and cut into transverse sections approximately 1 cm. in thickness. The usual yield was six sections, although the number varied from five to eight, depending on the size of the heart. A basal section, approximately 3 to 5 cm. in thickness, which included the aortic and pulmonary valves and the roots of the great vessels, remained. This was cut with a knife into multiple sections so that no recent or old infarcts might be overlooked. The basal (proximal) surface of each section was photographed in such a way that in the finished picture the anterior wall was below, and the left ventricle to the right (Figs. 2, 5, 8, 10).

Blocks for histologic study were cut from all diseased areas, as well as from representative portions of each ventricle and from the interventricular septum, regardless of the appearance to the naked eye. In every case at least one micro-

*The records were therefore taken and the letters Q, R, and S assigned to the initial ventricular deflections as in the paper by Kossmann and Johnston,[5] which deals with the curves obtained by means of the same special leads in a series of normal subjects. It has been recommended by the Committee on Precordial Leads of the American Heart Association that the galvanometer connections be made in the opposite way, so that positivity of the exploring electrode will be represented by an upward, instead of a downward, deflection. Since the letters Q, R, and S have been assigned as if the curves were reversed, the individual QRS deflections in our figures bear the names recommended by the committee. An initial summit is Q, a depression is R, and a summit preceded by a depression is S. With this nomenclature the RS or intrinsicoid deflection[6] is analagous to the intrinsic deflection[7] of direct leads.

scopic section of the aorta and one section of the auricular muscle were made. Duplicate sections were stained with hematoxylin and eosin and with a combined van Gieson-Weigert elastic tissue stain. A few were stained for fat with sudan III.

In Case 2, the relationship of each of the precordial leading-off points to the heart was ascertained by introducing a blunt probe perpendicular to the chest wall before the autopsy was performed. Figs. 5 and 6 show where the probe pierced the heart.

REPORT OF CASES

CASE 1.—C. A., a man 66 years old, first noted symptoms of diminished cardiac reserve in January, 1935, following an upper respiratory infection, and on April 13, 1935, he had symptoms of coronary occlusion. When he was admitted to the hospital

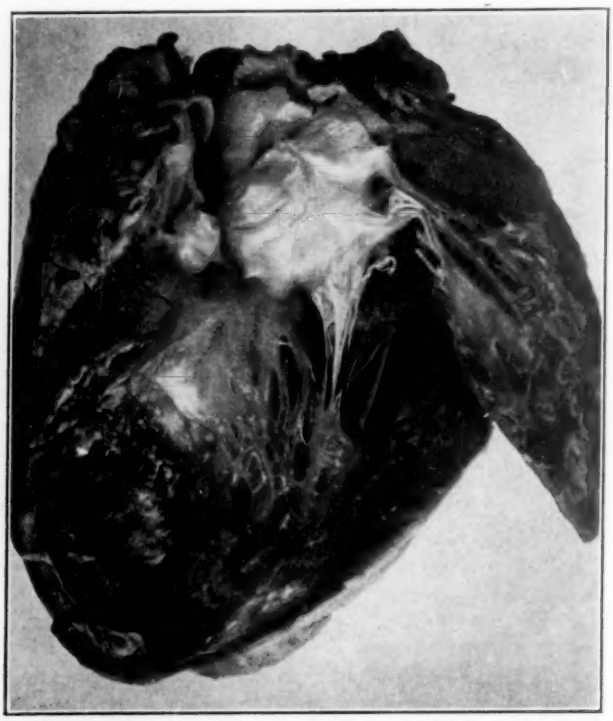

Fig. 1.—Case 1. Photograph of heart looking into the cavity of the left ventricle. The anterior wall is to the left. Old thrombus can be seen adherent to the interventricular septum, anterior wall, and entire apex. Scarring and thinning of the underlying myocardium are visible. Thickened endocardium shows as an irregular white line.

April 20, 1935, he had moderate congestive heart failure with pronounced mental symptoms, e.g., lethargy, dullness, disorientation, and memory defects. The heart was slightly enlarged, and the sounds were distant. There was a systolic murmur at the apex and another in the aortic area. The precordium seemed to be tender to pressure. The heart was beating regularly 100 times a minute. The blood pressure was 140/106. The mean blood pressure over a period of a month (daily measurements) was 138/90. A blood Wassermann test was negative.

The heart failure was progressive. Beginning April 23, the patient was digitalized rapidly and thereafter given 3 grains (2 cat units) daily. Fluids were administered parenterally, and the blood nonprotein nitrogen, which was 60 mg. per cent on admission, fell to 32 mg. per cent, but the patient developed decubitus

ulcers and Cheyne-Stokes respiration, and died of pulmonary edema May 25, 1935, five months after the first symptoms of heart disease, and forty-two days after the onset of symptoms of coronary occlusion.

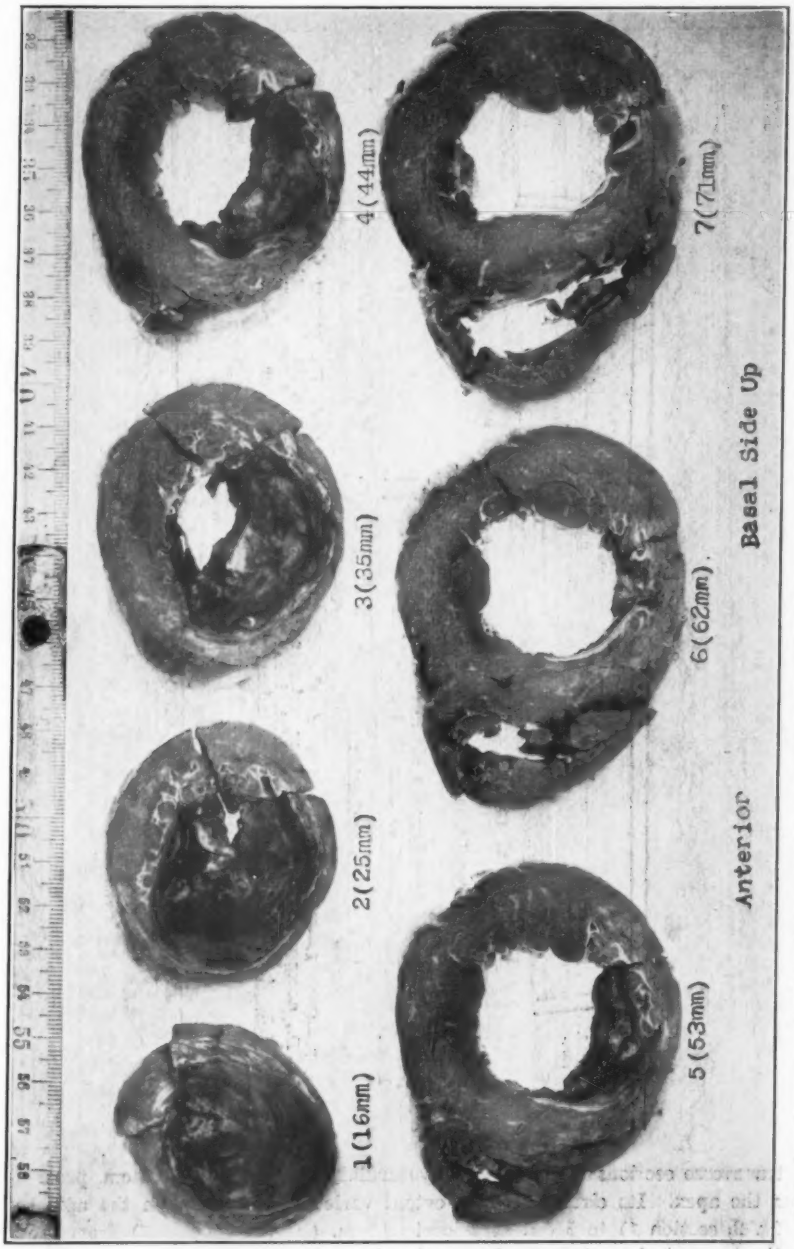

Fig. 2.—Same heart as in Fig. 1 (Case 1) cut into transverse sections, which are numbered consecutively from apex to base. The basal side of each section has been photographed with the anterior wall below, with the exception of section 1, which is rotated slightly in a counterclockwise direction. The number in parentheses under each section indicates its distance in millimeters from the apex of the heart. The intraventricular thrombus is dark in color and fills the apical sections. Note limitation, both of the thrombus and of the scarring, to the anterior wall of the left ventricle and adjacent septum, as the base is approached. Thickened endocardium can be seen as an irregular white line between the scarred myocardium and the intraventricular thrombus.

Necropsy.—The heart weighed 490 grams. The pericardial surfaces were smooth except near the apex, where there was an area of fibrinous exudate measuring 3 cm. × 3 cm. The valves of the heart and all of its chambers, except the enlarged left ventricle, were normal. The myocardium of the lower two-thirds of the anterior

portion of the interventricular septum and the apical one-third of the anterior left ventricular wall was replaced by firm, grayish-white tissue measuring about 4 to 6 mm. in thickness and located approximately 5 mm. subjacent to the epicardium. The endocardium of this area was thickened and covered with a large, firmly adherent, grayish-red thrombus of irregular outline (Figs. 1 and 2).

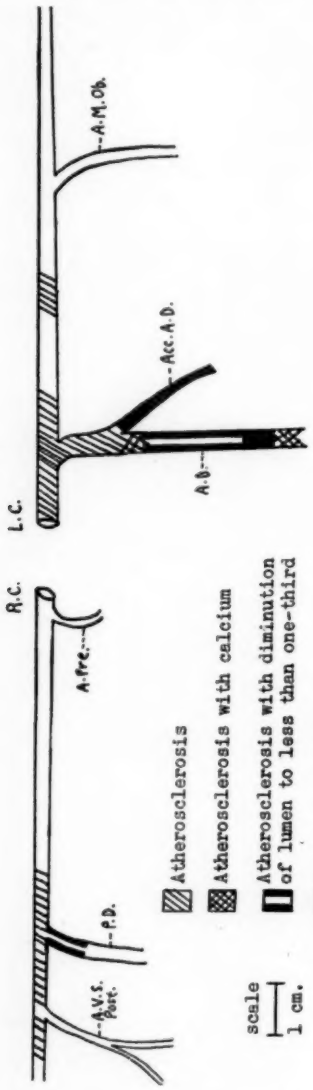

Fig. 3.—Case 1.—Coronary arteries. *L. C.*, left coronary artery; *A. D.*, ramus descendens anterior; *Acc. A. D.*, accessory ramus descendens anterior; *A. M. Ob.*, ramus marginis obtusae; *R. C.*, right coronary artery; *A. Pre.*, ramus anterior (preventricular); *P. D.*, ramus descendens posterior; *A. V. S. Post.*, ramus ventriculi sinistri posterior. Lesions are indicated by the code in the lower left-hand corner.

In the transverse sections (Fig. 2) the myocardial infarct extended 7 cm. proximally from the apex. Its circumferential extent varied from 10 cm. in the apical section (Fig. 2, section *1*) to 5 cm. at a level 62 mm. (Fig. 2, section *6*) from the apex. In the two apical sections the infarct involved almost the entire thickness of the anterior and lateral walls of the left ventricle, only 1 to 1.5 mm. of subepicardial muscle remaining. In the more proximal sections the area of infarction was confined to the anterior wall of the left ventricle and to the left side of the anterior portion of the interventricular septum (Fig. 2, sections *5*, *6*, and *7*).

Endocardial sclerosis was prominent over those portions of the left ventricle involved by the infarct. The right ventricle was unchanged.

Histologic examination of tissue removed from the transverse sections verified the macroscopic findings. Most of the infarct in the left ventricle was healed. In its peripheral portions organization was still in progress.

Macroscopic examination of the coronary vessels revealed marked atherosclerotic changes of the right and left coronary arteries and their branches (Fig. 3).

Microscopic examination indicated that the occlusion of the ramus descendens anterior 3 cm. from its origin was due either to eccentric intimal hyperplasia or to an organized thrombus. In its accessory branch a recent thrombus occluded the greatly narrowed lumen. The ramus descendens anterior was obviously the vessel of supply in the infarcted area.

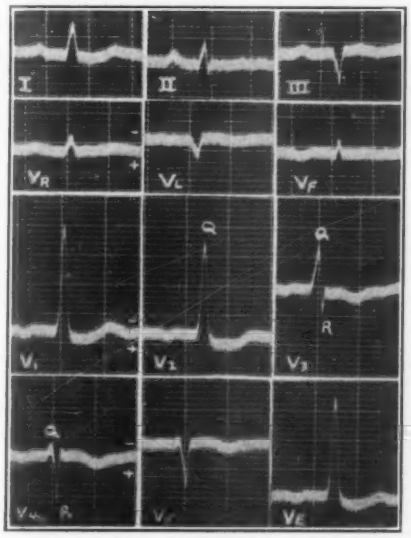

Fig. 4.—Standard electrocardiograms (I, II, III), extremity potentials (V_R, V_L, V_F), and precordial potentials (V_1, V_2, V_3, V_4, V_5, V_E) in Case 1, taken seventeen days after the onset of symptoms typical of coronary occlusion. The patient was completely digitalized. The standard leads and extremity potentials were recorded with the string at normal sensitivity; the precordial potentials were recorded at half-normal sensitivity (1 cm. = 2 mv.). An upward deflection in the special electrocardiograms represents relative negativity of the exploring electrode. Initial ventricular deflections are named, therefore, in a reverse manner (see footnote on p. 701). Time lines occur every 0.2 sec.

Unless otherwise stated, the symbols, string sensitivity, connections to galvanometer, and time lines are the same in all subsequent electrocardiographic illustrations.

Electrocardiograms.—Nine standard electrocardiograms were obtained, all of which showed sinus rhythm, low amplitude of both the initial and final ventricular deflections, and inversion of T_3. Curves taken after April 23 showed some depression of RS-T in Leads I and II, but this was probably due to digitalis and was not great, as comparison with the curve taken before the institution of therapy showed.

Precordial and extremity potentials were recorded on April 30, 1935, seventeen days after the probable date of coronary occlusion, seven days after digitalis was begun, and twenty-five days before

death. These are shown with the standard leads obtained on that date in Fig. 4. The extremity potentials, V_R, V_L, V_F, are of low amplitude. Also, as would be expected from the degree of left axis deviation shown in the standard leads, the potential of the left arm is positive and that of the left leg negative during the inscription of the initial ventricular deflections.

The precordial potentials (V_1, V_2, V_3, V_4, V_5, V_E) are distinctly abnormal. All of the initial ventricular deflections begin with a negative wave, Q. In Leads V_4 and V_5 this is small and not definitely outside normal limits. From points on the right side of the precordium (V_1, V_2, V_E) it is the only QRS deflection. In Lead V_3 it is followed by a small positive deflection, R. The final ventricular deflections are abnormal in the leads from the right side of the precordium, but little significance can be attached to this abnormality because the patient was completely digitalized.

CASE 2.—J. McE., a white male vagabond 54 years of age, had eaten irregularly for a year. There were no indications of heart disease until Feb. 8, 1936, when at 1:00 P.M. symptoms typical of coronary occlusion became manifest. He was admitted to the hospital February 9. The principal physical findings were malnutrition, enlargement of the heart, and marked sclerosis of the peripheral vessels. The heart was beating regularly at a rate of 88 per minute. On admission, the blood pressure was 128/88, and the mean of seven blood pressure readings was 136/89.

A teleoroentgenogram made on February 18 showed enlargement of the heart and sclerosis of the aorta. The erythrocyte count was 2,330,000, and the hemoglobin 58 per cent (Dare). A blood Wassermann test was negative.

Signs of congestive heart failure, which were absent on admission, developed rapidly with the patient at rest in bed. Digitalis, first administered February 18, produced only slight and temporary improvement. Shortly before death, icterus, hypothermia, and signs of cerebral anoxemia developed. Death occurred on February 23 from congestive heart failure, fifteen days after the onset of symptoms of coronary occlusion.

Necropsy.—The heart weighed 480 gm. The pericardium was normal. All of the valves and chambers were normal except the left ventricle, which was moderately dilated and hypertrophied, measuring 16 mm. in thickness at the base. Its anterior wall and the adjacent anterior portion of the interventricular septum were mottled in appearance, and distinctly softer and thinner than the rest of the myocardium. The columnae carneae were flattened. The infarct extended from a level 2 cm. below the mitral ring to within a centimeter of the apex.

Examination of the transverse sections (Fig. 5) revealed that the area of softening and mottling (outlined by broken white lines in the figure) extended from the apical level to within a few centimeters of the base of the heart, 8 cm. in all. In the apical section (Fig. 5, section *1*) it involved practically the entire circumference of the left ventricle. Proximally, the circumferential involvement diminished, i.e., to 8 cm. in section *3*, 6 cm. in section *4*, and 1 cm. in the basal section. In the apical sections the infarct was largely subendocardial, becoming more intramuscular at higher levels but not reaching the epicardium at any point. Sections *3*, *4*, *5*, and *6* showed distinct thinning of the anterior part of the septum, and in the last section the adjacent anterior walls of both the right and left ventricles were considerably thinner than usual.

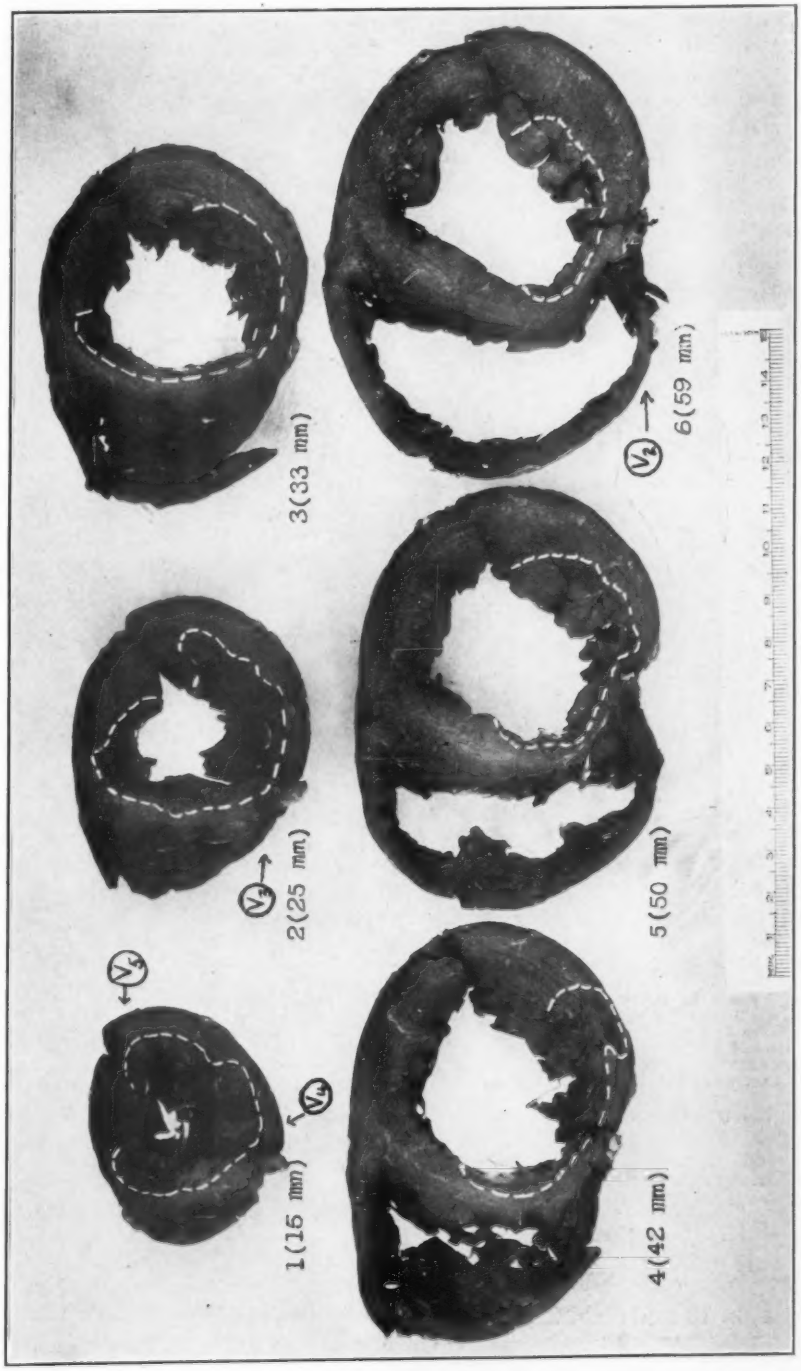

Fig. 5.—Case 2. Sections of the heart. The basal side of each section is seen, with the anterior wall below. The subendocardial extent of the infarct is outlined in white. The sections are numbered from apex to base. The figure in parentheses after each number indicates the distance in millimeters of that level from the apex. V_2, V_3, V_4, and V_5 show where a probe pierced the heart when introduced perpendicular to the chest wall at the following precordial points: V_2, the upper angle made by the junction of the fifth left rib with the sternum; V_3, fifth intercostal space in the left parasternal line; V_4, fifth intercostal space in the left midclavicular line; V_5, upper border of the sixth rib in the left anterior axillary line.

Histologic examination of the transverse sections revealed a recent, organizing infarct involving the area described. A small mural thrombus was seen in an apical section. In all sections the epicardium was thickened, except over the posterior wall of the left ventricle and over the right ventricle, and consisted of widely separated collagen fibers; many injected vessels and diffuse lymphocytic infiltration were also present. In a section through the lateral wall of the left ventricle fibrin was present on the epicardium, and there were a few invading histiocytes, but the infarcted area did not extend to the epicardium.

The area not involved by the infarct contained scattered foci of interfascicular and interstitial fibrosis. There were numerous arterioles which showed considerable reduplication of the internal elastic layer.

Gross and microscopic examination of the coronary arteries (Fig. 6) revealed severe atherosclerosis. The ramus descendens anterior of the left coronary artery

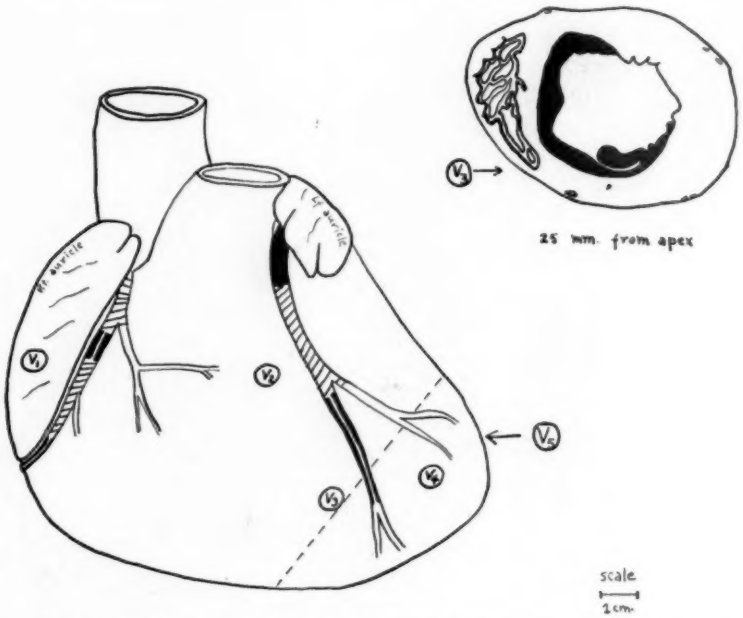

Fig. 6.—Diagrammatic representation of heart and coronary arteries in Case 2. Lesions in the arteries are indicated by the code used in Fig 3. V_1, V_2, V_3, V_4, and V_5 indicate where a probe which was pushed perpendicularly through the chest wall at the same precordial points from which Leads V_1 through V_5 were recorded (see Fig. 5) pierced the epicardium. When the probe was introduced at the ensiform process, it did not touch the heart. Inset in the upper right-hand corner is the section obtained by cutting through the dotted line shown near the apex. It corresponds to section 2 of Fig 5. The infarct is represented on it by solid black. The figure is intended to show particularly the spatial relationship to the heart of the precordial point used to record Lead V^3 (fifth intercostal space in the left parasternal line).

beginning at a point a few millimeters beyond its origin was occluded by a recent thrombus, 2 cm. long. The lumen of the right coronary artery was reduced in places to slitlike proportions.

Electrocardiograms.—Four standard electrocardiograms were taken between Feb. 10 and Feb. 22, 1936. All showed sinus rhythm and left axis deviation. The initial ventricular deflections were similar in all, exhibiting low amplitude with a small Q-wave, and a small slurred R-wave in Lead I; a prominent S-wave was present in Leads II and

III. The T-wave was inverted in Lead I in all curves, but in Leads II and III it varied a little, finally becoming upright as indicated in Fig. 7. The electrocardiograms, in short, showed a Q_1T_1 pattern, with a small Q_1.

The extremity and precordial potentials (Fig. 7) were recorded on Feb. 22, fourteen days after the appearance of symptoms of coronary occlusion, and one day before death. In the preceding four days the patient had received 21 grains (13 cat units) of digitalis by mouth. A study (unpublished) which we have made on the effect of digitalis on precordial potentials leads us to think that this amount probably had little effect on the final ventricular deflections in this case. The

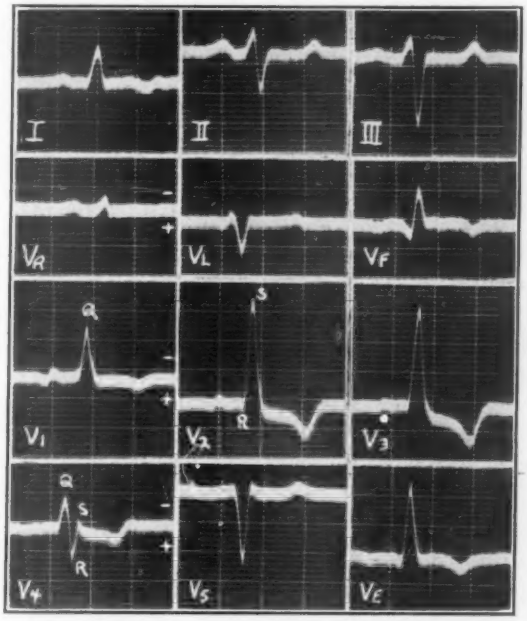

Fig. 7.—Case 2. Standard and special electrocardiograms recorded fourteen days after the occurrence of coronary occlusion.

minor changes in the T-waves in the standard leads following digitalis therapy support this belief.

The extremity potentials were of the type seen with left axis deviation. However, in contrast to Case 1, the potentials of the left arm and left leg showed small initial deflections opposite in direction to the chief deflection. Stated symbolically, V_L showed a small Q followed by a prominent R, and V_F showed a small R followed by a prominent S.

The precordial potentials were similar to those of Case 1 with the following differences: In Leads V_2, V_3, and V_E, there was a small initial positive deflection (R-wave); Lead V_4 was similar to Lead V_3 in Case 1, and both were similar to curves obtained experimentally[1]

from the margin of a recent infarct; there was considerable positive displacement of RS-T in Leads V_2 and V_3, less in Lead V_4; in Lead V_5 the T-wave was negative (upright).

CASE 3.—J. M., a white man 41 years of age, was a chronic alcoholic who had been drinking steadily for four or five weeks. The patient's personal history was unreliable, but apparently he had had temporary edema of the face and feet in November, 1935.

He was drunk when he was admitted to the Bellevue Psychiatric Pavilion Jan. 10, 1936, and had edema of the ankles, enlargement of the liver, and evidence of peripheral neuritis. The edema was thought to be nutritional because he had hypoproteinemia, a low or inverted albumin-globulin ratio on various occasions, and a history of inadequate diet. After four days of rest and an adequate diet the edema disappeared, and the patient was allowed out of bed. On January 20 he was observed to have dyspnea and cyanosis, during which he complained of pain over the precordium and his blood pressure fell. He passed through several similar episodes in the next few days. Signs of congestive heart failure appeared, and on January 25 he was digitalized. During that day he expectorated blood. Several subsequent hemoptyses were interpreted as indicating pulmonary infarctions.

Four roentgenograms taken at different times showed enlargement of the heart, dilatation of the aorta, and bilateral pleural effusion. The pleurae were tapped on several occasions. A blood Wassermann test was negative.

Signs of heart failure persisted. The pleural effusions became purulent, and cultures of the fluid revealed streptococcus viridans. The patient died of congestive heart failure and chronic bilateral empyema May 27, 1936, four months after the onset of symptoms of myocardial infarction.

Necropsy.—The heart, which weighed 480 gm., was greatly dilated, especially the left auricle. The mitral orifice measured 11 cm. and its valves showed moderate, diffuse thickening. The chordae tendineae and papillary muscles were prominent. The endocardium of the left ventricle was smooth except at the junction of the anterior wall and the interventricular septum, where it was thickened and overlaid by a grayish-red, firmly adherent thrombus. A small area of endocardium over the apical portion of the posterior wall presented the same changes.

Examination of the transverse sections (Fig. 8) showed the endocardium as an irregular, broad, white band over the areas mentioned. Small patches of adherent thrombus were seen over these areas. In section *4* (30 to 40 mm. from the apex) the endocardium appeared as dense white tissue, 2 mm. in thickness, from which bands of similar tissue extended into the myocardium. The muscle thus delimited presented a yellowish-gray mottled appearance. This zone measured 3 × 4 mm. Similar but smaller areas were seen in the corresponding portions of proximal sections (Fig. 8, section *6*).

Histologically, scarring of the endocardium, together with superimposed organizing mural thrombi, was seen, and there were several corresponding subendocardial foci of necrosis in the myocardium. Both walls contained dense, avascular, collagen scars, chiefly subendocardial, which represented healed infarcts. In one of the anterior wall scars two arterioles, occluded by canalized thrombi, were seen.

Macroscopic and histologic examination of the coronary arteries revealed mild focal atherosclerosis. At the origin of the ramus descendens posterior (of the right coronary artery) there was eccentric atherosclerosis which involved a few millimeters of its course and diminished its lumen by one-half. The left coronary artery

was thin-walled and patent, but its ramus descendens anterior showed in the first centimeter of its course a large, eccentric, yellowish-white plaque which narrowed the lumen considerably.*

Electrocardiograms.—Ten standard electrocardiograms, all showing sinus rhythm, were recorded at intervals of approximately ten days. Only the first, taken Jan. 24, 1936, was obtained before any digitalis had been given. Its deflections were of low amplitude in all leads, but displayed a Q_1T_1 pattern. All subsequent standard leads were similar to those shown in Fig. 9, which was taken February 18. The

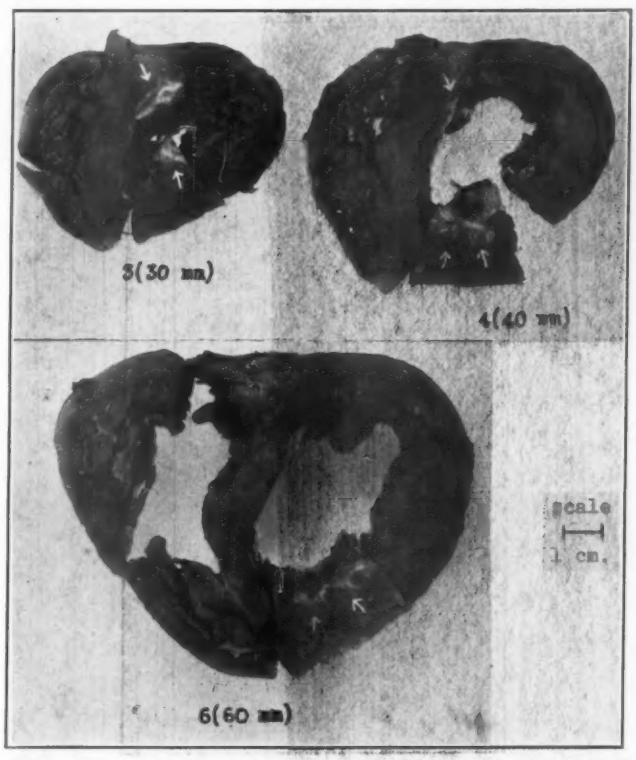

Fig. 8.—Sections of the heart in Case 3. Only three of the seven which were obtained are shown. Basal surfaces are seen with anterior wall below. The location of the thickened endocardium and the thin layer of subendocardial fibrosis are indicated by white arrows.

initial ventricular deflections were of abnormally small amplitude. In Lead III the chief, and usually the sole, initial deflection was downward, but in a few electrocardiograms this was preceded, and in one it was followed, by a small summit. The RS-T segment was slightly depressed in Leads I and II. The T-wave was low or isoelectric in all leads.

*The unusual features of this case were myocardial infarction without coronary occlusion, and bilateral empyema associated with multiple necrotic pulmonary infarcts. The latter has been discussed elsewhere.[8]

The extremity and precordial potentials were obtained twenty-nine days after the probable date of myocardial infarction. Although the amplitude of QRS was small in both, the relatively small size of the R-wave in leads from the first four precordial points was the striking feature. In Lead V_5, R was preceded by a small Q-wave.

The form of the initial ventricular deflections meant little because the patient was fully digitalized when the special curves were recorded.

CASE 4.—C. W., a man 76 years of age, had suffered since 1928 from postprandial pain which radiated to the chest. May 24, 1936, he was awakened from

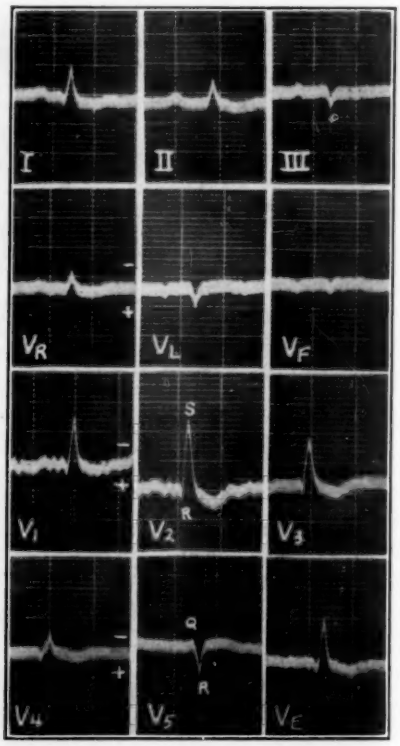

Fig. 9.—Case 3. Standard and special electrocardiograms recorded twenty-nine days after the probable date of myocardial infarction. The coarse oscillations in Leads V_1 and V_2 are artifacts. The patient was completely digitalized.

his sleep by symptoms which were suggestive of coronary occlusion. The next day, after the symptoms had abated, he entered the hospital. Roentgenologic examination showed that his heart was enlarged. The ventricular and pulse rates were 84 per minute. The blood pressure on the day of admission was 200/115, but fell five days later to 120/80, where it remained. There was no evidence of congestive heart failure. A blood Wassermann reaction was negative.

The patient's two months' stay in the hospital was uneventful except for brief precordial and epigastric pains radiating down the left arm on June 5 and again on June 12, 1936. On each occasion there was a leucocytosis and moderate rise in temperature.

The patient returned to the hospital Sept. 17, 1936, complaining of "epigastric distress" which disappeared after two weeks of rest in bed, and again Nov. 15, 1936, with symptoms and signs of congestive heart failure. Digitalis was given

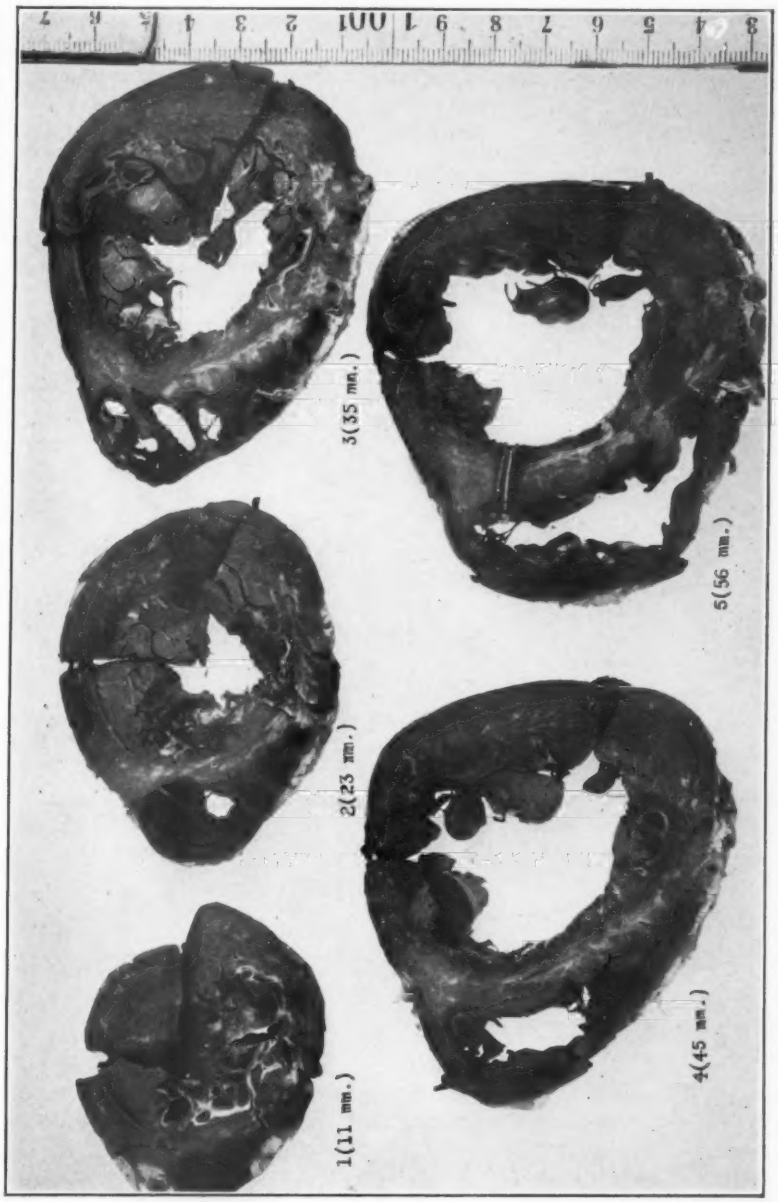

Fig. 10.—Sections of the heart in Case 4. In each, the basal side is up and the anterior wall is below. Note the pale, patchy scarring of the interventricular septum and adjacent anterior wall in all sections. In the first four sections thickening of the endocardium and an overlying adherent mural thrombus are visible. The transverse line over the posterior portion of the interventricular septum in section 5 is an artifact.

without benefit. Death occurred Nov. 28, 1936, five months after the first signs of coronary occlusion.

Necropsy.—The heart weighed 450 gm. The anterior wall of the left ventricle was the seat of many healed infarcts. Most of the midportion of the anterior three-fourths of the interventricular septum was replaced by a healed infarct (Fig.

10). Microscopically, healed lesions as well as recent subendocardial changes were found in the posterior wall of the left ventricle. The latter were seen only in the basal half of the heart, whereas the healed infarcts of the anterior wall and of the interventricular septum were found at all levels from apex to base (9 cm.). Organized mural thrombi were present in the anterior and septal walls of the left ventricle and in both auricles. The coronary arteries were sclerotic. The right coronary and ramus descendens of the left were almost completely occluded just beyond their origins. There was moderate narrowing throughout the entire extent of the circumflex branch of the left coronary artery. No recent or organized thrombi could be identified.

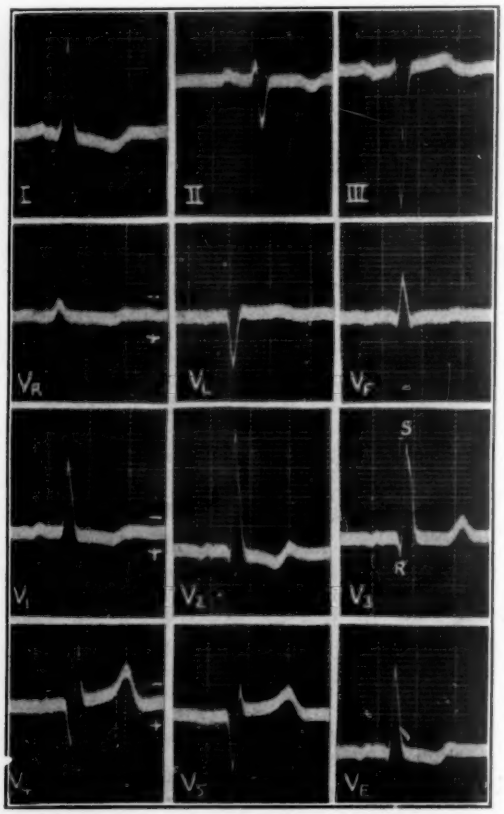

Fig. 11.—Case 4. Standard and special electrocardiograms recorded five days after the occurrence of coronary occlusion.

Electrocardiograms.—Twenty-four standard electrocardiograms, the first on May 25, 1936, were recorded during the three hospital admissions. All showed sinus rhythm and marked left axis deviation. In general, they were similar to the curve shown in Fig. 11, except that after the first electrocardiogram the amplitude of the initial ventricular deflections diminished. The QRS interval was 0.1 sec. in the curve shown in Fig. 11, but it increased later. During the last month of life, before any digitalis had been given, the P-R interval increased from about 0.16 or 0.17 sec. to 0.19 or 0.21 sec.

The extremity and precordial potentials were taken five days after the coronary occlusion and five months before death (Fig. 11). The potential of the left arm was positive, and of the left leg, negative, during the inscription of QRS. The precordial potentials were unusual. The R-wave was absent in Lead V_1, which was abnormal. The R-wave in Leads V_2, V_3, and V_E were abnormally small, and the S-wave in Leads V_2 and V_3 abnormally large, as judged by the criteria of Kossmann and Johnston. The RS deflection in all leads was within normal limits, however. The negative displacement of RS-T in Lead V_4, the negative T-wave in Leads V_3, V_4, and V_5, and the diphasic T in Lead V_2 were abnormal.

DISCUSSION

The Precordial Leads.—The deviations of the precordial electrocardiogram from normal in experimental and clinical myocardial infarction have recently been summarized by Wilson.[3] Experimental results in the early and late stages are quite constant, although acceptable explanations for some of the phenomena observed are lacking. The work of Wilson, Hill and Johnston[1] on dogs makes the following facts available: (1) Direct leads from infarcted areas which extend through the entire thickness of the ventricular wall yield curves which are characterized by a large initial negative deflection, Q, followed by a shallow, rounded, positive RS-T and T. Absence of the normal initial positive deflection (R-wave) is due to absence of electrical forces normally contributed by the involved muscle. For the sake of convenience this curve may be called the "central" type since it is obtained over the center of an infarct. (2) Curves obtained by direct leads from regions in which only the inner layers of muscle are infarcted may have a QRS group conforming to one of several patterns. It may consist of a single negative deflection, Q, with a prominent notch on its second limb. The notch may extend beyond the base line, in which event an R-wave and a true intrinsicoid[6] or RS deflection is present. In curves of the latter type the final negative deflection is occasionally missing, leaving only Q and R. In areas yielding curves of these types the RS-T segment is usually flat, and the T-wave is negative and prominent. These changes in the final ventricular deflections are attributed to disturbances affecting the recovery process in damaged muscle at the margins of the infarct. They are seen during subacute stages of infarction and are temporary. These several varieties of curves may be called "marginal" types because they are obtained by leading from the margin of an infarct. (3) Electrocardiograms similar in form to those described are obtained when the exploring electrode is separated from the epicardial surface of the heart by a gauze pad wet with physiologic saline or by the tissues of the chest wall.

The precordial electrocardiograms in our first two cases are similar in many respects to the various experimental curves described by Wilson, Johnston, and Hill. In the first case (Fig. 4) Leads V_1, V_2, and V_E are similar to direct leads from the center, and Lead V_3 is similar to a direct lead from the margin, of an infarct. The latter consists of a large Q, a small R, and an intrinsicoid deflection which just returns to the base line, so that an S-wave is absent. The small Q-wave in Leads V_4 and V_5 is not quantitatively beyond normal limits.[5] Digitalis probably had considerable effect upon the final ventricular deflections. However, it is to be noted that the position of the RS-T segment and the position of the apex of T are both reversed in Leads V_4 and V_5 as compared with Leads V_1 and V_2.

In the second case (Fig. 7) Leads V_2, V_3, and V_E, which are of the "central" type, differ from those in the previous case in that they show a small R-wave. This deflection sometimes occurs in direct leads from the center of an infarct,[1] but its origin is not known. A "marginal" curve, in this instance with an S-wave, is seen in Lead V_4. The abnormally positive RS-T segments in Leads V_2 and V_3 are in striking contrast to the relatively normal ones in the standard and extremity leads. The "marginal" curve (V_4) has a positive T, but its form is transitional between the relatively normal positive T in leads from points farther to the right and the abnormal T in Lead V_5 farther to the left.

An interesting observation in these two cases is that an infarct which was limited to the left side of the interventricular septum and to the anterior wall and apex of the left ventricle yielded chest leads of the "central" type, especially over the right side of the precordium. This, together with the fact that we had observed similar curves in a large number of cases diagnosed clinically as coronary occlusion, led us to perform the previously described probing experiment at necropsy in Case 2 in an effort to ascertain the anatomical relationship of the precordial points to the heart surface (Figs. 5 and 6). At the left sternal edge and in the left parasternal line (Leads V_2 and V_3) the probe entered the heart at the base and at the apex of the right ventricle, respectively; in the midclavicular line and in the anterior axillary line (Leads V_4 and V_5) it pierced the apex of the left ventricle; at the right sternal edge (Lead V_1) it entered the right auricle; and at the tip of the ensiform (Lead V_E) it did not touch the heart at all. Admitting that certain errors exist in such a procedure, it seems certain that the first three leads (V_1, V_2, V_3) were semidirect leads from areas of the heart surface to the right of the anterior interventricular groove.

The explanation for the "central" type of potentials in leads from the right half of the precordium in cases without infarction of the right ventricle is lacking, but, when this matter is considered in the

light of other observations, we suspect that such curves are due to the fact that infarction of the left side of the anterior interventricular septum has destroyed the electrical forces normally contributed by that side.

Whatever the correct explanation may be, the subject has considerable practical importance, for occasionally the R-wave is missing in Leads V_1, V_2, and V_E, and is small in midprecordial leads in cases with marked left ventricular hypertrophy.[9, 10] The precordial potentials in cases of myocardial infarction can usually be differentiated from these by the similar absence of the R-wave in one or several of the remaining leads or by the presence of a "marginal" pattern in one of these leads; furthermore, in acute and subacute stages of anterior infarction the special electrocardiograms may frequently show an abnormal T-wave different from that seen in left ventricular hypertrophy.

The last part of this statement may be amplified by considering the chest leads in Case 4 (Fig. 11). The abnormalities of the initial ventricular deflections, including the absence of a true intrinsicoid or RS deflection in Lead V_1, are not specific, for, as already noted, they are seen in cases of left ventricular hypertrophy. The weight of the heart was 450 gm., and hypertrophy of the left ventricle was moderate. It was doubtful, therefore, if these changes were independent of the infarct. The abnormal final ventricular deflections, on the other hand, are similar to those obtained after recent infarction of the anterior heart wall and are unlike those encountered in left ventricular enlargement. With the latter, a negative T-wave is found only in those curves obtained from precordial leads well to the left, where the R-wave is of considerable magnitude. In the case under discussion an abnormal T-wave occurred with a small R-wave in Leads V_2 and V_3. Presumably, more definite changes in the initial ventricular deflections were absent because the infarct was located well back in the septum, was patchy in distribution, and was well surrounded by normal muscle fibers, especially in its anterior portion.

The third case (Figs. 8 and 9) is unusual in several respects. The important abnormalities of the special electrocardiograms are the small R-wave in leads from the midprecordium, and the short RS deflection in Leads V_4 and V_5. The T-wave is abnormal on the left, but at least part of this abnormality can be attributed to digitalis.

It may be worth while to speculate on the cause of the small R-wave. Since in direct or semidirect leads this deflection depends on electrical forces generated by the passage of excitation through the adjacent ventricular wall,[11] it might, theoretically, be diminished in at least three ways: (1) by functional reduction of these forces, (2) by replacement of large numbers of muscle fibers by fibrous tissue, and (3)

by subendocardial infarction of such limited degree and extent as to diminish or delay the electrical forces normally contributed by the involved muscle. Ordinarily a direct lead in the region of such an infarct yields a "marginal" type of curve with a prominent initial negative deflection.[1] In the circumstances hypothesized, it might give an R-wave of small size. In the present case it seems that the sclerosis of the endocardium with involvement of a thin layer of adjacent myocardium, principally in the anterior wall of the left ventricle, and the multiple foci of scarring in the same region are sufficient to account for the observed diminution of the R-wave. One cannot be sure that these are the only factors, for the chest wall lies at some distance from the epicardial surface, and the effect of the variables which this spatial relationship introduces has not been ascertained. The miliary foci of necrosis seen at necropsy are of no significance so far as the curves presented are concerned, for the latter were recorded three months before death.

If the possible factors listed in the preceding paragraph are actually operative, it would appear that the abnormalities in the chest leads in Case 3 are not specific for myocardial infarction. In support of this contention we may refer to another case, not included here, in which the precordial potentials were very similar to those shown in Fig. 9. At necropsy the myocardium was the seat of advanced perivascular and interfascicular fibrosis caused by progressive coronary atherosclerosis and presumably by previous rheumatic infection. It is therefore possible for a small initial positive deflection to occur in leads from the middle or left side of the precordium when there is diffuse replacement fibrosis of the underlying ventricular wall. Obviously, the importance of being able to differentiate this clinically from a small subendocardial infarct is negligible.

The infarct in Case 2 was subendocardial, involving in most locations half or less of the thickness of the ventricular wall (Fig. 5). The chest leads showed a small R-wave in Lead V_2 and Lead V_3 (Fig. 7). The theory advanced above does not satisfactorily explain this small R-wave because it does not account for a typical "marginal" type of curve in Lead V_4. Moreover, it was shown at necropsy in Case 2 that the two leads mentioned were probably semidirect leads from the right ventricle. This, as indicated earlier, further complicates the matter. For the present, the facts must be accepted without complete explanation.

The Relative Value of Leads From One or Several Precordial Points.—It is well-known that infarction of the myocardium occasionally causes characteristic changes in the initial and final ventricular deflections of the precordial electrocardiogram when such changes are partially or completely absent from the standard leads.[12] It is not

so well-known that such changes are frequently definite at several precordial points and absent or indefinite at others. If a single apical lead had been taken with a small exploring electrode, the curve obtained in all of the four cases presented would have been similar to that from the anterior axillary line (Lead V_5), because the apex beat was well beyond the midclavicular line. In all four cases this lead is nearly the same (Figs. 4, 7, 9, 11). The abnormal T-wave indicates merely an abnormal recovery process which might be due to almost any cause whatsoever, including digitalis medication, while the QRS group, consisting principally of a large R-wave, gives no hint of the degree of pathologic changes which are clearly reflected in leads taken further to the right in three of the cases. The small Q-wave of this lead in Cases 1 and 3 is within normal limits.[5] It would seem that the six leads used in the present work are not necessary in every case, but it is nevertheless clear that a single apical lead must often give incomplete or inconclusive information.

SUMMARY

The potential variations of the extremities and of six precordial points were correlated with the pathologic changes in four cases of infarction principally of the anterior wall of the left ventricle and, with one exception, of the anterior portion of the interventricular septum.

In the precordial electrocardiograms "central" and "marginal" patterns of the initial ventricular deflections similar to those obtained by Wilson, Johnston, and Hill in direct and semidirect leads in experimental infarction were easily recognized. The necropsy observations, however, indicate that several factors in addition to those held responsible for such curves in animals are probably of importance in human subjects.

In cases of infarction of the myocardium the additional and more conclusive information given by several leads, as compared with a single precordial lead, is made evident.

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ACCURACY IN DIAGNOSIS AND LOCALIZATION OF MYOCARDIAL INFARCTION*

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THIS report is a correlation of the clinical, electrocardiographic, and pathologic observations in thirty-four cases of acute myocardial infarction studied at Lakeside Hospital. Special consideration has been given to the validity of the electrocardiographic evidence, both as to diagnosis and localization of the infarcts, and to errors in interpretation.

The subject of electrocardiographic changes in acute experimental and clinical myocardial infarction has been reviewed by Crawford and his coworkers,[1] Barnes,[2] Wolferth,[3] and Wilson and his associates.[4, 5, 6] Post-mortem examination of the heart in cases of myocardial infarction occasionally reveals no obstruction of major arteries. The area of infarction, therefore, is of prime importance, and the electrocardiographic diagnosis must relate to the area, rather than to occlusion of any particular coronary artery. The single infarctions are usually located in (1) the anterior, lateral, and apical part of the left ventricle (usually caused by obstruction of the anterior descending branch); (2) the posterior and basal portion of the ventricles (usually caused by obstruction of the left circumflex branch and occasionally by occlusion of the right coronary artery or the right descending branch); and (3) the interventricular septum (supplied by the septal branches of the right and left coronary arteries). Acute infarcts may be single or multiple, and may occur in hearts which are already the seat of old infarcts.

EXPERIMENTAL CORONARY ARTERY OCCLUSION

The electrocardiogram of acute experimental occlusion is characterized by a monophasic S-T and in many instances by the appearance of Q or an increase in the depth of an already existing Q. The infarct may be localized by studying the pattern of the changes in the Q-wave and S-T segments. Septal infarcts are often betrayed by prolongation of the P-R interval, dropped beats, A-V block, bundle branch block, or intraventricular block. The electrocardiographic changes caused by experimental occlusion of specific arteries are given in Table I.

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TABLE I

ELECTROCARDIOGRAPHIC PATTERNS FOLLOWING CORONARY ARTERY OCCLUSION

ARTERY	PROLONGED A-V CONDUCTION PROLONGED INTRAVENTRICULAR CONDUCTION	Q_1	Q_3	S-T DEVIATION	CHEST LEAD (UPWARD DEFLECTION +)
			Experimental		
Left descending branch	Infrequently	+	0	Ld. I + Ld. III −	QRS: initial wave deeply negative S-T deviation +
Left circumflex branch	Occasionally	0	+	Ld. I − Ld. III +	QRS: normal S-T deviation −
Right coronary artery	Occasionally	0	+	Ld. I − Ld. III +	QRS: normal S-T deviation −
Septal branch of left coronary artery	Left bundle branch block A-V block a late effect	0	0	Ld. I + Ld. III −	QRS: normal S-T deviation +
			Clinical		
Left descending branch (Anterior, apical, lateral portion of the left ventricle)	Infrequently	+	0	Ld. I + Ld. III −	QRS: initial wave deeply negative S-T deviation +
Left circumflex branch (Posterior and basal portion of left ventricle)	Occasionally	0	+	Ld. I − Ld. III +	QRS: normal S-T deviation −
Septal branch of right circumflex artery (Septal infarct)	Occasionally	0	+	Ld. I − Ld. III +	QRS: normal S-T deviation −

Clinical Electrocardiographic Evidence of Infarction.—Herrick,[7] in an important paper, described the clinical and electrocardiographic signs of acute coronary occlusion. It remained for Pardee[8] to re-emphasize the importance of the electrocardiographic evidence and to study the localization of the infarcts on the basis of previous experimental work. In one of his cases there was pathologic confirmation of the electrocardiographic diagnosis, both as to the presence and location of the infarct. Pardee was the first to correlate the location of the infarct in the heart with the electrocardiographic pattern.

Parkinson and Bedford[9] classified the electrocardiographic changes in their cases of recent coronary thrombosis as R-T_1 or R-T_3, depending on the characteristic elevation of R-T in the named lead of the standard electrocardiogram. They also divided the T-wave changes occurring two or three weeks following the infarction into T_1 and T_3 types, depending on whether T was negative in Lead 1 or Lead 3. In four of their cases autopsy confirmed their diagnoses. Wilson[5] divided the changes into Q_1 and Q_3 types: Q_1 associated with anterior infarctions and Q_3 with posterior infarctions. Barnes,[2] in an extensive study of autopsy cases, found that it was possible to localize the infarcts with great accuracy. He concluded that the R-T_1 type was initiated by anterior and apical infarcts (caused by occlusion of the anterior descending branch), and that the R-T_3 type was caused by posterior and basal lesions, the result of occlusion of either the right coronary artery or the circumflex branch of the left coronary artery.

Wolferth and Wood[10] increased the accuracy of electrocardiographic diagnosis, including localization, by the use of chest leads. In a recent report Wolferth[11] presented the electrocardiographic changes due to combinations of anterior and posterior infarcts, showing that the effect of the anterior infarct predominated and that the elevation of R-T_2 was greater than that of R-T_1.

Septal infarcts usually produce electrocardiograms showing various stages of A-V heart block or bundle branch block. Gross[12] stated that the upper septal branch comes from the right circumflex artery and anastomoses with the corresponding branch of the left coronary artery. He also stated that the right bundle branch is supplied invariably by one of the earliest branches of the anterior descending branch of the left coronary artery, and that the left bundle branch has no specific blood supply. White[13] reported bundle branch block as one of the rapid changes in the electrocardiogram in a case of recent coronary thrombosis.

Table II correlates the electrocardiographic patterns in our cases with the location of the occlusions and infarcts.

Judging from experimental and clinical studies of recent myocardial infarction, a correct diagnosis and an accurate localization may be

TABLE II

CASE	ECG. DIAGNOSIS	AREAS OF ACUTE INFARCTION	AREAS OF OLD INFARCTION	ARTERIES THROMBOSED
1.	Ant. and apical	*B. proteus* abscess in anterior and apical portion of lt. ventricle		None
2.	Post. and basal (c)	Left ventricle. Ant. and post. at base. Upper ⅓ of septum	Left ventricle ant. and post. Focal in upper ⅓ of septum	*Recent* in rt. and left circumflex coronary. *Old* in right coronary
3.	Anterior (c)	Lower ⅓ of left vent. ant. Lower ⅓ of septum	In rt. and lt. vent. post.	*Recent* in ramus desc. of left. *Old*, right coronary artery
4.	Anterior	Lower ⅓ of lt. and rt. vent. ant. Entire septum		*Recent*, left coronary
5.	Anterior (b)	Lower ⅔ of lt. vent. ant. Lower ⅓ of rt. vent. ant. Ant. lower ⅓ of septum	Ant. left vent.	*Recent* in ramus descendens of left coronary *Old* in ramus descendens of left coronary
6.	Posterior		(3 mo.) at post. wall of left vent. at apex	None
7.	Anterior (d)	Lower ⅓ of lt. vent. anterior Focal in septum	Upper ⅓ of lt. vent. Post. upper post. ⅓ of septum	*Old*, right coronary *Old*, ramus descendens of left coronary
8.	Anterior	Lower ⅔ of lt. vent. ant. Entire septum	Lower ⅓ of lt. vent. ant. Lower ⅓ of rt. vent. ant.	*Recent*, ramus desc. of left coronary *Old*, right coronary
9.	Anterior Septal (b) (a)	Lower ⅔ lt. vent. ant. Lower ⅔ lt. vent. post. All of septum	Focal of rt. vent. ant. and post.	*Recent*, ramus desc. of left coronary *Old*, right coronary
10.	Anterior Posterior (e)	At tip of lt. and rt. vent. ant. At tip of septum Below sulcus lt. vent. post.		*Recent*, small branches (microscopic)
11.	Anterior (c)	Lower ⅓ of lt. vent. ant. Ant. lower ⅓ and post. upper ⅓ of septum Upper ⅓ lt. vent. post. Right auricle lat. portion—micro.	Lower ⅓ of lt. vent. ant.	*Remota*, ramus descendens of left coronary

(a) Left bundle branch block
(b) Intraventricular block
(c) Auricular fibrillation
(d) No chest lead
(e) Prolonged P-R interval

TABLE II—CONT'D

CASE	ECG. DIAGNOSIS	AREAS OF ACUTE INFARCTION	AREAS OF OLD INFARCTION	ARTERIES THROMBOSED
12.	Posterior Septal	At base of left vent. post. Upper portion of septum	Multiple of lt. vent. ant. Multiple of lt. vent. post.	*Recent*, right coronary *Old*, left circumflex and ramus descendens of left coronary
13.	Anterior	Lower ⅔ of left vent. ant. Lower ⅔ of septum	Upper ⅓ lt. vent. post. Focal of lt. vent. ant. Post. of upper ⅓ of sept.	*Recent*, ramus descendens of left coronary *Old*, right coronary
14.	Anterior	Lower ⅓ of lt. vent. ant. Lower ⅓ of rt. vent. Lower ⅓ of septum	Focal and mult. of lt. vent. ant. Focal and mult. of lt. vent. post.	*Recent*, ramus descendens of left coronary *Old*, right coronary
15.	Posterior	Upper ⅓ of lt. vent. post.		*Recent*, left coronary
16.	Anterior	Lower ⅔ of lt. vent. ant. Lower ⅔ septum Lower ⅔ lt. vent. post.	Focal of lt. vent. post. Focal of septum	*Recent*, ramus descendens of lt. coronary *Old*, right coronary
17.	Anterior	Lower ⅔ lt. vent. ant.	Diffuse of lt. vent. ant.	*Recent*, ramus descendens of lt. coronary
18.	Anterior	At apex of lt. vent. ant. Tip and margin of septum		*Recent*, ramus descendens of left coronary
19.	Anterior	At apex of lt. vent. ant. with rupture Lower ⅓ of septum		*Recent*, ramus descendens of lt. cor. *Recent*, lt. circumflex
20.	Anterior	At apex of lt. vent. ant. At apex of rt. vent. ant. Ant. apical portion of septum		*Recent*, ramus descendens of lt. coronary
21.	Posterior	Post. wall of lt. vent. post. representing the lesion responsible for the recent infarction		*Recent*, right coronary *Old*, right coronary *Old*, left circumflex
22.	Posterior Septal	Multiple throughout both vent. and septum		*Recent*, right coronary *Recent*, left coronary
23.	Posterior (c) (d)	Posterior wall of lt. vent. post. and postpapillary muscle	Fibrous of lt. and rt. vent. ant. and post.	*Recent*, almost complete atheromatous occlusion near origin of right coronary *Old*, marked coronary sclerosis

TABLE II—CONT'D

CASE	ECG. DIAGNOSIS	AREAS OF ACUTE INFARCTION	AREAS OF OLD INFARCTION	ARTERIES THROMBOSED
24.	Anterior	At apex of lt. vent. ant.	Posterior wall of lt. vent.	*Recent,* ramus descendens of left coronary *Old,* right coronary
25.	Anterior	Apical region of lt. vent. ant. Almost entire septum		*Recent,* 8 cm. from origin of ramus descendens of lt. coronary
26.	Post and basal	Post. portion along margo obtusus of l.v. from base to apex	Throughout l.v. from base to apex show small scarred areas	Marked sclerosis, tip of l. cor. In places less than 1 mm. in diameter
27.	Anterior and apical	L.v. ant. with area 2 cm. in diam. of softening at apex. Mural thrombus on endocardium at this site	Throughout entire l.v. is the seat of old fibrosis	In descendens just after its division from lt. cor. a large calcified plaque was found and lumen at this point was less than 1 mm. Immediately distal to the plaque the artery was occluded for 1 cm. by a white atheroma
28.	Posterior and basal	In posterior wall of rt. vent. near post. portion of septum an area of 2.5 cm. Posterior one-half of septum from base to apex		None

attained in a high percentage of cases. The infarcts may be localized clinically as anterior, posterior, combined anterior and posterior, septal, and auricular, and the vessel which is occluded may often be named, but there are cases in which the thrombosis involves only the arteriolar supply of the area infarcted, leaving the large vessels patent. Arterial anomalies may likewise introduce errors. Abscesses and metastatic tumors of the heart may produce electrocardiographic changes resembling those of infarction.

METHOD OF TAKING ELECTROCARDIOGRAMS

The records include the conventional leads in all cases and, in most instances, chest leads. The latter were taken from the fifth left costal cartilage and from the apex, using the right arm wire for the exploring electrode and the left leg wire for the indifferent electrode. Following Wilson's method, we have recently changed the connections so that an upright deflection now indicates relative positivity of the precordial electrode. We have been using the left arm wire for the exploring electrode and the right arm wire for the indifferent electrode. In four instances a complete precordial survey was made by the technique of Wilson,[14] employing the central terminal for the indifferent electrode (R.A., L.A., and L.L.).

Thirty-four cases of acute myocardial infarction, in which the diagnosis was substantiated at autopsy, were studied. There were twenty-nine males and five females. Four patients were colored. In three instances electrocardiograms had been taken previous to the occurrence of the infarct. The electrocardiographic diagnosis of recent infarction was correct in twenty-eight cases (82.05 per cent). (Table III.)

TABLE III

RÉSUMÉ OF THE PATHOLOGIC FINDINGS

AREAS OF INFARCTION	PATH. LOCALIZATION	ECG. LOCALIZATION	ERRORS*
Anterior	6	4	2 (Cases e and f)
Posterior	5	5	
Anterior and posterior	1		1 (Case b)
Anterior and septal	13	1 (10 diagnosed anterior)	2 (Cases c and d)
Posterior and septal	2	1 (1 diagnosed posterior)	
Anterior, posterior, and septal	4	1 (diagnosed ant. and post.) 2 (diagnosed post. and septal)	
Anterior, posterior, septal (basal and apical)	1	1 (diagnosed posterior and septal)	
Anterior and posterior at apex and septal and auricular	2	1 (diagnosed anterior, Case 11) 1 (diagnosed posterior and septal, Case 10)	

*These cases are discussed separately later in this paper.

Table IV shows which arteries were thrombosed. The frequency of multiple thromboses is evident. Infarction of the right auricle occurred in two cases (Cases 10 and 11). In Case 11, auricular fibrillation with frequent ventricular extrasystoles was present. There was also infarction of the anterior lower third and of the posterior upper third of the interventricular septum. In addition, there was old and recent infarction of the lower third of the left ventricle anteriorly, and recent infarction in the upper third of the left ventricle posteriorly. A partially occlusive thrombus was found in the anterior descending branch, midway between its origin and the apex, together with severe generalized coronary arteriosclerosis. In Case 10 the electrocardiogram (Fig. 1) shows regular sinus rhythm, sinus arrest, ventricular escape, and prolongation of the P-R interval. T_1 is tall and peaked; S-T_2 and S-T_3 are monophasic; and Q_3 is abnormally deep. Lead IV, taken from the fifth left costal cartilage, shows a deeply negative monophasic S-T. Lead V, from the apex, shows an elevated and monophasic S-T with a sharply negative T. The chests

TABLE IV

INCIDENCE OF THROMBOSIS IN THE CORONARY ARTERIES IN 34 CASES

OCCLUSION OF RIGHT CORONARY NEAR ORIGIN		OCCLUSION OF LEFT CORONARY NEAR ORIGIN		OCCLUSION OF ANTERIOR DESCENDING BRANCH		OCCLUSION OF LEFT CIRCUMFLEX BRANCH		SMALL ARTERIES SUPPLYING ANTERIOR PART OF APICES OF BOTH VENTRICLES AND ADJACENT SEPTUM. UPPER POSTERIOR SURFACE OF LEFT VENTRICLE		GENERALIZED SEVERE CORONARY SCLEROSIS
OLD	RECENT	OLD	RECENT	OLD	RECENT	OLD	RECENT	OLD	RECENT	
Case 13	Case 2	Case 12	Case 22	Case 7	Case 3	None	Case 2	None	Case 10	Case 6
Case 14	Case 9		Case d	Case 11	Case 4		Case 15			Case 7
Case 16	Case 12			Case 12	Case 5		Case 19			Case 11
Case 24	Case 21			Case e	Case 8		Case 21			Case 23
Case b	Case 22				Case 9		Case f			Case a
	Case b				Case 13					Case f
					Case 14					Case 26
					Case 16					
					Case 17					
					Case 18					
					Case 19					
					Case 20					
					Case 24					
					Case 25					
					Case c					
					Case e					
					Case 27					
Number of Thromboses in Each Coronary Artery										
5	6	1	2	4	17		5		1	7

leads (IV and V) were recorded with the right arm wire attached to the exploring electrode. Autopsy showed that there was a recent infarct of the lower third of the anterior portion of both ventricles and the tip of the septum. There was another infarct in the posterior and central portion of the heart involving the left ventricle and

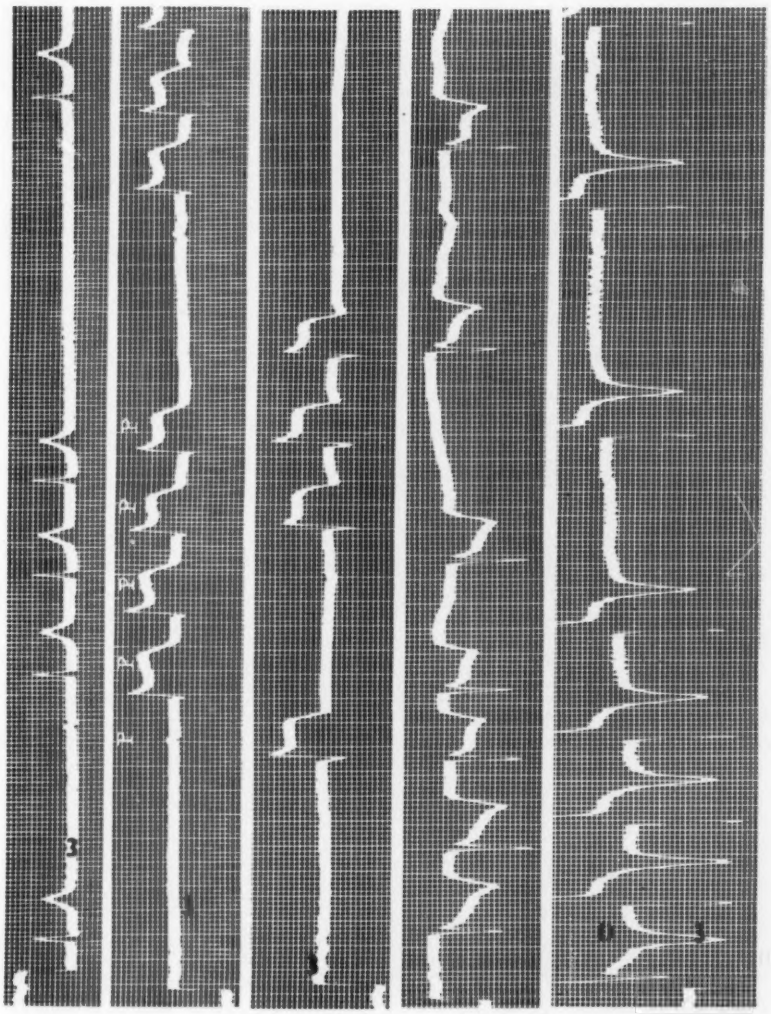

Fig. 1.—Case 10, see text.

septum. There was clotted blood, much of which was hyalinized, in the interstices of the muscle bands of the right auricle. The small coronary twigs in this area showed marked sclerosis and thickening.

Cardiac Rhythm.—Regular sinus rhythm was found in 27 cases; ventricular extrasystoles were present in 7 cases; and auricular fibrillation was present in 5 cases, 2 from the beginning of the infarction and 3 during the progress of the illness. A-V nodal rhythm occurred

in 2 cases; in one of these it was replaced by regular sinus rhythm, and in the other it changed to auricular fibrillation. Auricular flutter occurred in one case, to be superseded later by normal rhythm.

Axis Deviation.—Left axis deviation occurred in 18 cases, right axis deviation in one case, and no axis deviation in 15 cases.

Conduction Defects.—Complete A-V block occurred in one case; intraventricular block, in 4 cases; left bundle branch block, in 4 cases; and right bundle branch block, in one case.

Value of Chest Leads.—In 4 cases the diagnosis could be made by chest leads alone. In none of the cases were the chest leads normal. Of 28 cases in which the electrocardiographic diagnosis was confirmed post mortem, the conventional leads were diagnostic in 19. In 4 of these cases the chest leads (from the fifth left costal cartilage and from the apex) made the electrocardiographic evidence more convincing. Evidence of posterior infarction was obtained more frequently in the lead from the fifth left costal cartilage, and of anterior infarction in that from the apex.

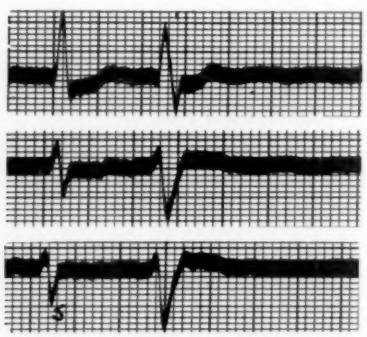

Fig. 2.—Case a, see text.

ERRORS IN ELECTROCARDIOGRAPHIC DIAGNOSIS

1. (Case a) M., aged 65 years, was admitted to the hospital because of congestive cardiac failure due to arteriosclerotic disease with moderate hypertension. The patient was digitalized and died of progressive failure on the fourth hospital day. The electrocardiogram (Fig. 2) showed auricular fibrillation, left axis deviation and frequent ventricular extrasystoles. There was nothing in the ventricular complex to suggest old or recent myocardial disease. Post-mortem examination: Heart weight, 445 gm.; old and recent infarction of the anterior and lower third of the interventricular septum and of the left ventricle near the apex. The anterior descending branch showed arteriosclerotic changes but no thrombosis. This error may have been due to the lack of chest leads.

2. (Case b) M., aged 61 years, was admitted to the hospital with congestive cardiac failure of eight months' duration. There was a history of retrosternal pain four days prior to admission to the hospital. The patient had been digitalized before admission. The clinical diagnosis was arteriosclerotic heart disease with hypertension, and diabetes mellitus. For four months the patient had slight precordial pain which radiated to his left arm. Four or five days previous to admission, he

became dyspneic and had precordial pain. There was slight peripheral edema. Blood pressure was 140/80. He received digitalis and salyrgan; on the third hospital day he was placed in an oxygen tent but died on the fourth hospital day. The electrocardiogram (Fig. 3*A*), taken one month before admission, showed left axis deviation, S-T_1 depressed 1.5 mm., S-T_2 depressed 0.5 mm., S-T_3 elevated 0.5 mm., and S-T_4 depressed 0.5 mm. (right arm wire exploring electrode and left leg wire indifferent electrode). An electrocardiogram taken on the second hospital day (Fig. 3*B*), showed normal sinus rhythm, left axis deviation, a P-R interval of 0.21 sec., S-T_1 depressed 1 mm., S-T_2 very slightly elevated, S-T_3 elevated 1 mm., notching of QRS in all leads, and a diphasic T-wave in the chest lead. The voltage was reduced. The definite changes in the second record, i.e., the elevation of S-T_2 and S-T_3 with depression of S-T_1, suggested posterior infarction, but this evidence was

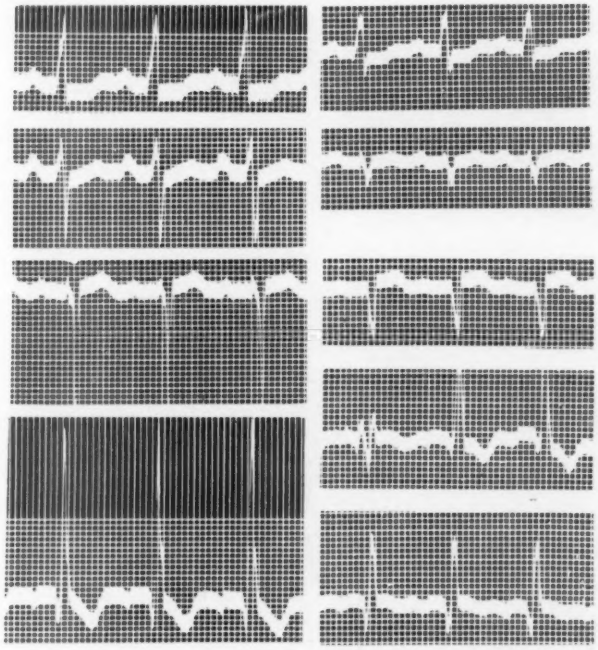

Fig. 3.—Case b, see text.

not sufficient for a positive diagnosis. At autopsy, the heart, which weighed 650 gm., showed mural thrombi in the right auricle and right ventricle, old fibrosis of the septum, a large infarction both old and recent in the posterior portion of the right ventricle near the base, and an old infarction with a recent spotty infarct of the right ventricle anteriorly. An old thrombus in the right coronary artery was overlaid by a recent occlusive thrombus. The right auricle was infarcted. Marked calcification and atheromatous changes were seen in the other coronary arteries. Although the electrocardiogram was not definitely diagnostic of recent infarction, the rapid change should have aroused strong suspicions.

3. (Case c) M., aged 59 years, was admitted to the hospital with an attack of severe dyspnea which had lasted three weeks. Substernal oppression occurred a few days before admission. The blood pressure was 180/140. On the fifth hospital day the patient died suddenly while expelling an enema. The electrocardiogram taken on the second day of hospitalization showed regular sinus rhythm and left bundle branch block (Fig. 4*A*). A second record taken on the fifth hospital day (Fig. 4*B*)

showed regular sinus rhythm. The bundle branch block had disappeared. Occasional ventricular extrasystoles were seen. The chest lead (anteroposterior) showed

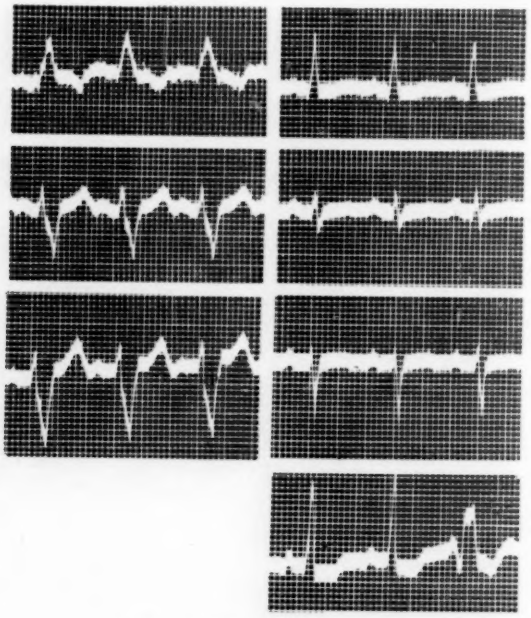

Fig. 4.—Case c, see text.

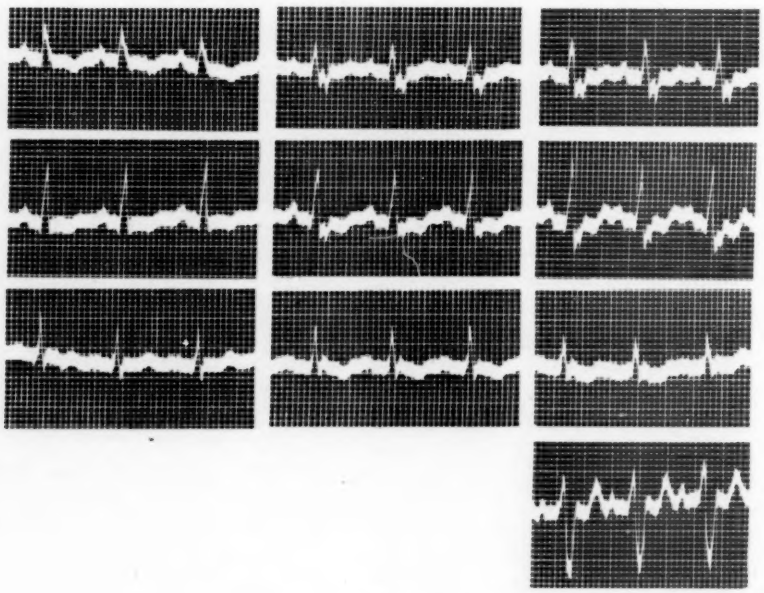

Fig. 5.—Case d, see text.

no Q-wave, and S-T was depressed 1.3 mm. The rapid changes in the electrocardiogram and the absence of Q_1 were diagnostic of recent infarction of the anterior surface of the heart. The temporary left bundle branch block was diagnostic of

septal infarction. Post-mortem examination revealed that the heart weighed 660 gm. Old and recent infarction of the septum (left side) and old and recent infarction of the anterior portion of the left ventricle were found. A recent thrombus was present in the anterior descending branch of the left coronary artery.

4. (Case d) M., aged 67 years, was admitted to the hospital because of severe retrosternal pain for eight hours. There was a history of postprandial retrosternal pain which had increased in frequency for a period of two years. On admission to

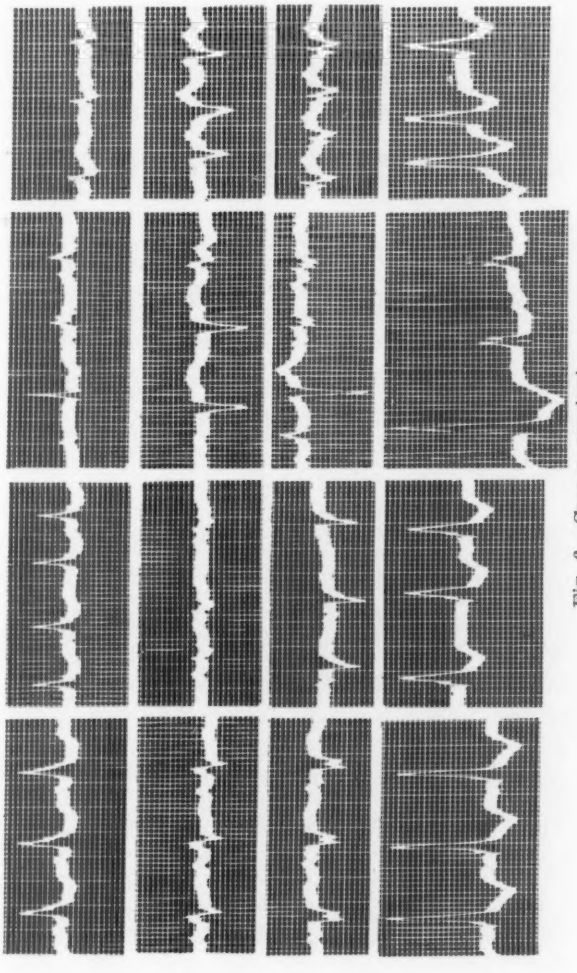

Fig. 6.—Case e, see text.

the hospital he had congestive cardiac failure. The blood pressure was 168/116. Death occurred on the seventh hospital day. The electrocardiogram taken on the first hospital day (Fig. 5*A*) showed regular sinus rhythm, widening of QRS_1, and a Pardee type $S\text{-}T_1$ and $S\text{-}T_2$ with inversion of T. No chest lead was taken. This record suggested a remote myocardial infarct, involving the anterior portion of the heart. A record taken on the third hospital day (Fig. 5*B*) showed regular sinus rhythm and defective conduction in the right bundle branch. The previously negative T_1 became positive. A record taken on the fifth hospital day (Fig. 5*C*) showed no changes in Leads I, II or III, but the chest lead (anteroposterior) showed no Q, and T was upright and tall. Clinically, this patient had coronary thrombosis, and

this diagnosis was confirmed by the rapidly changing electrocardiogram. This case might well have been included with those which were diagnosed correctly. Post-mortem examination showed that the heart weighed 500 gm. and that there were old and recent infarcts of the lower anterior third of the septum and of the lower half of the left ventricle anteriorly. A recent thrombosis was found in the anterior descending branch at its origin.

5. (Case e) F., aged 61 years, was admitted to the hospital for the first time because of cardiac decompensation. The clinical diagnosis was arteriosclerotic heart disease with hypertension (blood pressure, 170/115). The electrocardiogram showed regular sinus rhythm and left bundle branch block (Fig. 6*A*). The patient was digitalized and discharged as improved. Again, five months later, she was admitted because of cardiac decompensation and severe precordial pain. A friction rub was heard on the second hospital day. The patient had leucocytosis, a little fever, and

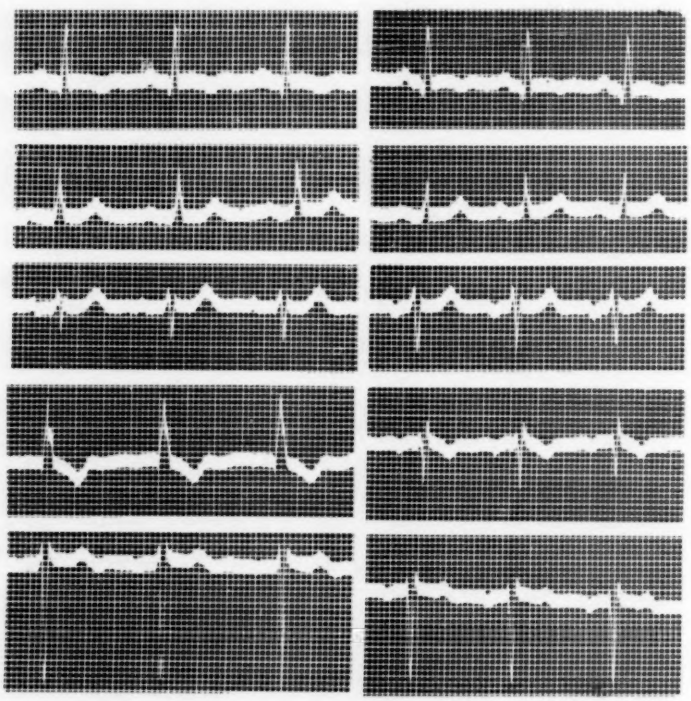

Fig. 7.—Case f, see text.

heart failure. A clinical diagnosis of old and recent myocardial infarction was made. The electrocardiogram showed wandering pacemaker and left bundle branch block (Fig. 6*B*). A record taken on the second hospital day showed, in addition, ventricular extrasystoles. Eleven days later there occurred a varying intraventricular conduction defect (Fig. 6*C*), and twenty-seven days later the record showed a striking change, again with evidence of intraventricular conduction disturbances (Fig. 6*D*). The congestive failure grew worse steadily, and the patient died one day after the last record was made. The post-mortem examination showed that the heart weighed 450 gm., and was the seat of diffuse myocardial fibrosis and a recent infarct at the tip of the left ventricle. An old and recent thrombus was found in the anterior descending branch 3 cm. from its origin.

6. (Case f) M., aged 60 years, was admitted to the hospital because of moderately severe substernal pain radiating to the left arm. The pain lasted three days.

Three years previously he had had an attack of indigestion which confined him to bed for two days. Subsequently the patient had been in good health. The clinical diagnosis at the time of this admission was arteriosclerotic heart disease with hypertension (blood pressure 190/110), coronary sclerosis, and recent coronary occlusion. The electrocardiogram on the first hospital day showed normal sinus rhythm and left axis deviation; Q_1 was present; S-T_1 was very slightly elevated; T_1 was inverted; and T_4 was upright. (The right arm wire was connected to the exploring electrode and the left leg wire to the indifferent electrode.) (Fig. 7*A*.) A diagnosis of myocardial disease was made. A record two days later (Fig. 7*B*) was much the same. The abnormalities were consistent with myocardial changes due to fibrosis, the result of remote coronary occlusion. The clinical diagnosis of recent coronary occlusion was not confirmed by the electrocardiogram. One day later the patient died suddenly. Post-mortem examination showed that the heart weighed 500 gm.; it was the seat of fibrosis in the greater part of the septum, and there was evidence of a remote infarct in the left anterior half of the septum; old and recent infarcts were found in the anterior surface of the left ventricle, and rupture of the myocardium through the central part of the infarct (over the anterior papillary muscle) had occurred. There was calcification of the left circumflex artery with recent thrombosis of the other coronary arteries.

DISCUSSION OF ERRORS

The records of patients with hypertensive arteriosclerotic heart disease, especially when digitalis has been administered, may be somewhat confusing. Atypical curves suggesting posterior and basal infarcts may be due to acute right ventricular strain caused by recent multiple pulmonary infarcts. In the curves of the latter condition there is a deep S_1, and the depression of S-T_1 and elevation of S-T_3 are not striking. In the chest lead the typical S-T deviation is not present (Barnes[15]). Pericarditis with and without effusion causes elevation of S-T, but this is usually present in all leads and there is no complementary depression. Likewise the chest lead is helpful, as it is not always monophasic. The history in all of the above conditions may assist in the diagnosis.

In six patients (Table V) having myocardial infarction at post-mortem examination, the electrocardiographic charges were not sufficiently definite to confirm the clinical diagnosis of coronary occlusion.

In summary, one error may have been due to lack of chest leads. In one case with successive records the diagnosis could not be made. In four cases there was suggestive evidence which, if taken with the history in three cases, should have led to the diagnosis of recent coronary thrombosis. In the one case in which successive records were made and no electrocardiographic evidence of recent coronary thrombosis was found, necropsy disclosed fibrosis of the septum, old and recent myocardial infarction near the base and old infarction of the right ventricle anteriorly, with recent spotty infarction in the same area. This anterior and posterior infarction of the right ventricle, both old and recent, may have been responsible for the absence of confirmatory electrocardiographic evidence. In none of the six cases was the electrocardiogram entirely normal.

TABLE V

CASE	ECG. DIAGNOSIS	AREAS OF ACUTE INFARCTION	AREAS OF OLD INFARCTION	ARTERIES THROMBOSED
a.	Auricular fib. with many vent. extrasystoles	Mural thromb. on septum Areas of myomalacia near apex region	Areas of old myomalacia near apex region	Sclerosis of ramus descendens of left coronary artery
b.	Changes in record suggested myocardial involvement but not conclusive for infarction	Right vent. post. and lateral—spotty infarction right vent. ant. Rt. auricle. Mural thrombi in right auricle and ventricle	Right vent. post. and lateral fibrosis of septum and right vent. ant.	*Recent*, right coronary; marked sclerosis of other coronaries
c.	Shifting pacemaker evidence of myocardial damage	Tip of lt. vent. ant.	Diffuse fibrosis through ant. heart	*Recent*, ramus descendens of lt. cor. *Old*, ramus decendens of lt. coronary
d.	1. Changed to normal 2. Sinus rhythm with depression $S\text{-}T_4$ (old method). Absence of of Q_4	Lower ⅔ of lt. vent. ant. and lt. side of septum	Lower ⅔ of lt. ventricle ant. and lt. side of septum	*Recent*, ramus descendens of lt. coronary
e.	1. Pardee $S\text{-}T_{1 \text{ and } 2}$ Inverted T_1 2. With upright T_1 3. With upright T_1 and absence of Q_4	Lower ½ of lt. vent. ant. and ant. lower ⅓ of septum	Lower ½ of lt. vent. ant. and ant. lower ⅓ of septum	*Recent*, ramus descendens of lt. coronary
f.	1. Inverted T_1 and upright T_4 2. Same as No. 1 and $S\text{-}T_1$ is Pardee type	Apex of lt. vent. ant. with rupture through central portions	At apex of lt. vent. Fibrosis of greater portion of septum	*Recent*, lt. circumflex *Old*, lt. circumflex

Infarction of the right ventricle (Table VI) alone occurred in only one case in this series. This patient had hypertensive arteriosclerotic heart disease with congestive failure. Angina played no part in the clinical picture. The electrocardiogram showed suggestive but not conclusive evidence of a posterior and basal infarct. The right coronary artery was obstructed 5 cm. from its origin by a recent organized thrombus which was superimposed on an older thrombus. In six cases acute infarction of the right ventricle occurred in combination with infarction of the left ventricle. In four of these, the left ventricle anteriorly and the septum were involved. In one case both the anterior and posterior portions of the left ventricle and the septum were infarcted. In this case the electrocardiographic diagnosis was posterior and septal infarction. In the remaining case the anterior portion of

TABLE VI

INFARCTION IN RIGHT VENTRICLE

CASE	RECENT INFARCTION		OLD INFARCTION	INFARCTION ELSEWHERE	ECG.
	ANTERIOR	POSTERIOR			
3.			At base of left and right vent. post.	Recent in ant. left vent. and septum	Anterior
4.	Multiple, lower ⅓			Recent lower ant. ⅓ of lt. vent. and entire septum	Anterior
5.	Multiple, lower ⅓			Recent lower ⅔ of lt. vent. and lower ⅓ of septum	Anterior
9.			At base of rt. vent. ant. and post.	Recent lower ⅔ of left vent. ant. and all of septum	Anterior and septal
10.	Multiple, tip of right vent.			Recent tip of lt. vent. ant. and post. Recent below sulcus of lt. vent. post.	Anterior and posterior
8.			Old lower ⅓ of rt. vent. ant.	Recent lower ⅔ lt. vent. ant. and entire septum	Anterior
14.	Multiple, lower ⅓ rt. vent.			Recent lower ⅓ lt. vent. ant. and lower ⅓ of septum	Anterior
20.	Multiple, apex			Recent at apex of lt. vent. ant. and apical portion of septum	Anterior
22.	Multiple	Multiple		Recent multiple of lt. vent. ant and post. and septum	Posterior and septal
23.			At base of rt. vent. ant. and post.	Recent of post. wall lt. vent. and post. papillary muscle.	Posterior
28.		Single, at base		Recent post. ½ of septum, base to apex	Posterior and basal
29.	Multiple, lower ⅓. Mural thrombi	Multiple, at base			In cases of error

the apex and the posterior surface of the left ventricle near the auriculoventricular sulcus were the seat of infarction. In the latter case the electrocardiogram fulfilled the criteria of Wolferth[11] (Fig. 1).

SUMMARY

Of 34 cases of recent myocardial infarction in which necropsy was performed, the clinical and electrocardiographic diagnosis was correct in 28 (82.05 per cent). In the 6 undiagnosed cases there was some electrocardiographic evidence in 3, and none in the other 3 cases. These diagnostic errors were due to lack of chest leads in one case, left bundle branch block in 2 cases, and intraventricular block in one case; in 2 cases the evidence was suggestive, but not conclusive. In 21 cases pericarditis was present at autopsy, but in none were the electrocardiographic changes typical of those seen in acute pericarditis.

Multiple acute infarction without previous infarction was present in 8 cases (24 per cent), and in 22 cases the recent infarction, both single and multiple, was associated with older infarction.[16*] In the case of acute single infarction alone the accuracy of diagnosis and localization was 100 per cent. In the cases of recent and old infarction accuracy of diagnosis and localization was 73 per cent. In the diagnosed cases the accuracy of the electrocardiographic localization of the major acute infarction was 100 per cent (28 cases).

The diagnosis of acute myocardial infarction should be made from the patient's history, the physical examination, and laboratory findings.[17] The electrocardiogram (especially when serial records and chest leads are taken) will assist in the diagnosis and localization of infarction in over 80 per cent of the cases.

We wish to thank Dr. A. R. Moritz, Pathologist of Lakeside Hospital, for his assistance in the analysis of the post-mortem data.

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*Right auricular infarction occurred in two cases.

Department of Clinical Reports

COARCTATION OF THE AORTA AT AN UNUSUAL SITE, ASSOCIATED WITH A CONGENITALLY BICUSPID AORTIC VALVE

REPORT OF CASE*

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COARCTATION of the aorta is one of the congenital anomalies which lends itself to precise recognition during life. The case which we are reporting not only emphasizes the salient features of coarctation of the aorta, but is of interest because the site of the narrowing bore an unusual relationship to the origin of the left subclavian artery. The exact anatomic diagnosis was made clinically despite the fact that evidence of collateral circulation could not be elicited. The clue, in fact, to the correct diagnosis was afforded by the unusual anatomic arrangement. The absence of corroborative signs was regarded as attributable in part, at least, to the extreme degree of circulatory failure present when the patient was first seen.

Coarctation of the aorta has been classified into the so-called adult and infantile types. The infantile form consists of a diffuse narrowing of the aorta between the origin of the left subclavian artery and the point of insertion of the ductus arteriosus. The ductus arteriosus remains patent, and the situation may be regarded as an exaggeration of the anatomic arrangement that exists normally in the fetus. The adult type of coarctation is rarely associated with a patent ductus arteriosus. The narrowing of the aortic isthmus is abrupt, and the degree of stenosis amounts in some cases to complete obliteration of the aortic lumen at the site involved, with the result that an extensive collateral circulation develops.

The pathologic changes and the theories of pathogenesis of this lesion have been adequately considered in the reviews of Bonnett,[3] Abbott,[1] Hamilton and Abbott,[5] and Blackford,[2] and it is unnecessary to discuss them here.

REPORT OF CASE

A man, twenty-six years of age, was admitted directly to the cardiac service at the Worrall Hospital in an obviously critical state of congestive failure. The details of his history were meager as well as difficult to obtain. He apparently had

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always experienced excellent health and had led a very active life, enjoying more than average physical strength and endurance, as was necessary in his occupation, which was that of a farm laborer. Three months before his admission to the hospital he first had noted moderate dyspnea on exertion and weakness of the legs. Both of these symptoms had become progressively more severe until two weeks prior to his admission to the hospital, when he had begun to have paroxysmal attacks of dyspnea, and edema of the legs had developed. Despite these symptoms of circulatory failure he had remained ambulatory until three days before his admission to the hospital. Approximately 60 minims (4 c.c.) of tincture of digitalis had been administered daily without benefit.

Physical examination revealed a well-developed and well-nourished young man. He was continuously orthopneic but had only slight cyanosis. The respiratory rate was between 40 and 50 per minute and the pulse rate was 120 per minute; there were visibly exaggerated pulsations of the carotid arteries. The temperature was 98.4° F. There was moderate edema of the legs, and the liver extended about 2½ inches below the costal margin. Coarse râles were present at the bases of both lungs. The heart was enlarged and the apical impulse was visible in the fifth intercostal space to the left of the anterior axillary line. The tones were of poor quality, and a definite gallop rhythm was present. A rough systolic murmur and a blowing diastolic murmur could be heard over the aortic area.

The finding of a marked disparity in the volume of the two radial pulses immediately aroused our attention. The pulse in the right radial artery was large and of a forceful "water-hammer" quality, whereas that in the left radial artery was so small as to be hardly palpable. The blood pressure in the right arm was 210/40 mm. Hg, and in the left arm, 100/78 mm. Hg. No pulsation could be felt in the abdominal aorta or in the arteries of the legs. Whereas the pulsations in both carotids and the right subclavian were very prominent, careful palpation over the left subclavian artery revealed almost no pulsation at all. Careful search did not disclose any evidence of increased collateral circulation.

Routine examination of the urine did not reveal any abnormality except moderate albuminuria (Grade 2). The concentration of hemoglobin was 11.9 gm. per 100 c.c. of blood; the erythrocytes numbered 3,540,000, and the leucocytes 24,100, per cubic millimeter of blood, respectively. The flocculation test for syphilis was negative. The value for the blood urea was 90 mg. per 100 c.c. Roentgenologic examination of the thorax did not reveal any evidence of erosion of the ribs. The heart was enlarged, there was congestion of the lungs, and the aorta appeared to be dilated. The electrocardiogram showed left ventricular preponderance, incomplete bundle branch block (QRS, 0.14 sec.), inverted P-waves in Lead III, and delayed A-V conduction (P-R, 0.28 sec.), and the Wolferth Lead IV showed inverted T-waves, diminished Q-waves, and notched QRS complexes.

The diagnosis was coarctation of the aorta at or above the level of the left subclavian artery, chronic rheumatic endocarditis, aortic insufficiency, and cardiac decompensation. The patient failed to respond to supportive treatment, and anuria developed. This was assumed to be secondary to circulatory insufficiency. The patient died on the fourth day after his admission to the hospital. In view of the post-mortem findings, it is interesting to note that he remained afebrile while under our observation. Necropsy disclosed marked enlargement of the heart, tremendous hypertrophy of the left ventricle, and dilatation of the right and left ventricles. The heart weighed 855 gm. An abrupt coarctation of the aortic isthmus was found, reducing the lumen at this point to only 8 mm. The aorta showed marked dilatation distal to the site of coarctation, but the proximal segment was smaller than normal. The ductus arteriosus consisted of a thick, firm, fibrous cord measuring 3 to 5 mm. in diameter; its lumen was completely obliterated, and its point of insertion

into the aortic wall was immediately proximal to the site of coarctation. The abnormally small left subclavian artery arose just distal to the coarctation, and the normal left carotid artery sprang from the arch of the aorta immediately proximal to the site of stenosis (Figs. 1, 2 and 3).

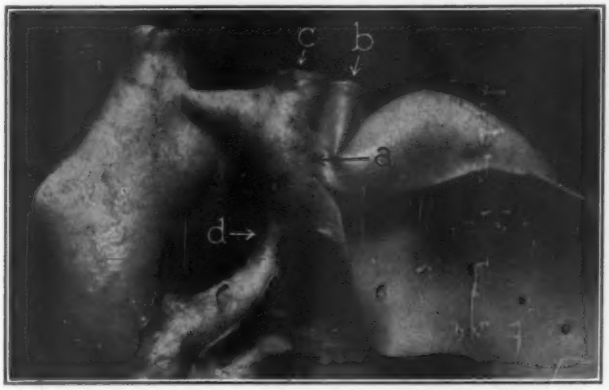

Fig. 1.—Coarctation of aorta showing relationship of aorta and vessels; *a*, site of coarctation; *b*, left subclavian artery; *c*, left common carotid artery; *d*, thickened and obliterated ductus arteriosus. The aorta distal to the coarctation is dilated and is relatively small proximal to it.

Fig. 2.—Coarctation of aorta (aorta and other vessels opened); *a*, thin constricting band arising above the subclavian artery; *b*, subclavian artery; *c*, left common carotid artery; *d*, site of attachment of the obliterated ductus arteriosus.

Examination of the heart disclosed a congenitally bicuspid aortic valve; both leaflets were involved in an extensive vegetative endocarditis. Fragile subacute vegetations covered the greater portion of both aortic leaflets and there had been

extension of the process along the adjacent endocardium of the left ventricle (Figs. 4 and 5). The mitral, tricuspid and pulmonary valves appeared normal. The heart measurements were as follows: Aortic valve 8 cm., mitral valve 12.5 cm., tricuspid valve 16 cm., pulmonary valve 10 cm. The depth of the left ventricle was 10 cm., and the thickness of its wall was 1.8 cm. The depth of the right ventricle was 12 cm., and its wall was 0.4 cm. thick. Both internal mammary arteries were appreciably enlarged, and there was a general increase in size of the intercostal vessels; there was also enlargement of the thymic artery. Complete necropsy did not reveal anything else significant except evidence of chronic passive congestion. The liver was enlarged and weighed 2280 gm., and the spleen weighed 455 gm. A small infarct was present in the right kidney and another was found in the base of the right lung. Examination of the brain did not reveal any evidence of embolism, or of congenital aneurysm of the vessels constituting the circle of Willis.

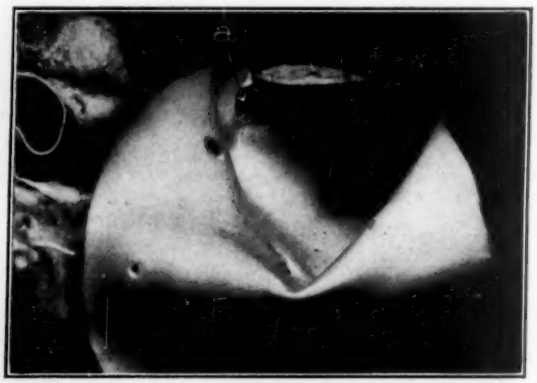

Fig. 3.—Coarctation of aorta; view of the aorta from below the coarctation, showing the marked degree of aortic constriction; the lumen at *a* measured 9 mm. in diameter.

COMMENT

The presence of high brachial arterial pressure without corroborative evidence of true essential hypertension is often the initial clue which leads to the diagnosis of coarctation of the aorta. The classic findings of elevated blood pressure in the upper extremities in contrast to a reduced pressure in the lower extremities, small or absent pulsations in the abdominal aorta and arteries of the legs, and associated evidence of collateral circulation in the upper part of the body are important criteria of coarctation. A significant disparity in the pulse volume and blood pressure in the two arms, however, has not been of frequent occurrence in proved cases of coarctation.

King[6] has made an exhaustive review of the blood pressure measurements in the reported cases of this anomaly. Of 175 cases, there were 66 in which the blood pressure in both arms was recorded. In only 10 of these was there an appreciable difference in the blood pressure in the two arms. Unfortunately, necropsy information was available only in the case reported by Woltman and Shelden.[7] The blood pressure in this case was 164/86 in the right arm, and 126/110 in the left arm.

Fig. 4.—Marked ventricular hypertrophy and dilatation contrasted with heart of normal size below; the fact that the aortic valve is bicuspid and is the seat of vegetative endocarditis is well demonstrated.

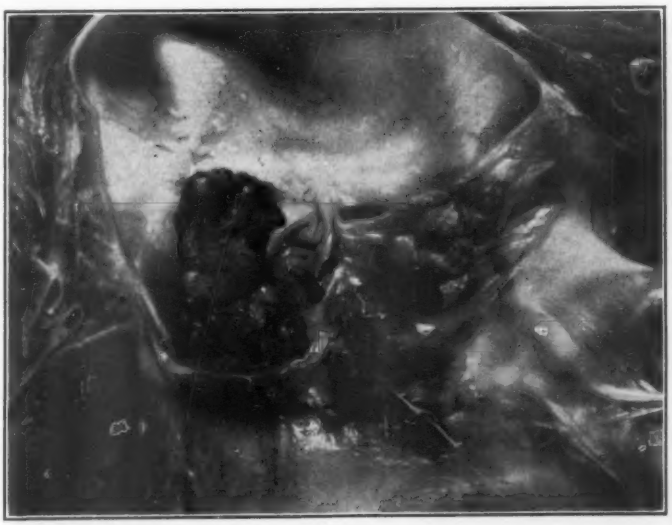

Fig. 5.—Close-up of the bicuspid aortic valve and vegetative endocarditis.

Necropsy disclosed that the proximal portion of the left subclavian artery consisted only of a fine ligamentous cord; the distal part of the artery was the recipient of extensive collateral vessels. In a recent case reported by Borgard[4] the clinical appearance was typically that of coaretation. In addition, there was associated evidence of obstruction to the left subclavian artery, from which he concluded that the site of coarctation was proximal thereto.

In Abbott's review[1] of 200 cases recorded in the literature, there were six in which anatomic study showed that the stenosis was definitely "above the ductus," and in seven others it was described as situated at or above the origin of the left subclavian artery. These figures would indicate that the anatomic relations which existed in our case are relatively rare.

One of the interesting features of our case was the presence of a congenitally bicuspid aortic valve. It is indeed not uncommon to find defects in the vascular system associated with coaretation. Bonnett[3] and Abbott[1] have called attention to the fact that the grave and complex forms of associated anomalies, such as biloculate or triloculate heart, transposition of the aortic trunks, and pulmonary atresia, are commonly combined with the infantile type of coaretation. The minor congenital variations, such as bicuspid aortic valve, anomalous origin of the arteries from the arch of the aorta, and defects of the aortic septum and subaortic stenosis, occur frequently in the adult type of coaretation. A congenitally bicuspid aortic valve was found in 25.1 per cent of Abbott's series of cases.

Another feature of interest in our case was the presence of subacute vegetative endocarditis of the bicuspid aortic valve. Although the presence of coexisting valvular disease and aortic insufficiency was diagnosed before death, we did not suspect the true nature of the lesion. The patient had remained afebrile, and except for the presence of leucocytosis, there was no indication of an inflammatory process. Furthermore, there was no clinical evidence of embolic phenomena. This again, however, must call our attention to the fact that the possible development of bacterial or vegetative endocarditis is one of the most constant hazards in congenital heart disease. One may well wonder whether the myocardium might have remained compensated if this lesion had not been present. Undoubtedly the degree of coaretation present in this case imposes a no small burden on the heart; yet in the presence of a normal myocardium without the superimposed inflammatory process, the heart in all probability would have carried this burden for many years without noticeable circulatory deficiency. Abbott's statistics show that the highest mortality occurs between the

second and third decades of life; however, cases in which the patients live beyond the fifth and sixth decades of life are not uncommon.

In cases of coarctation death usually results from progressive myocardial failure. Other common causes are rupture of the heart, rupture of the aorta, the development of an aneurysm, either aortic or cerebral, and endocarditis.

SUMMARY

We have reported a case of coarctation of the aorta in which the site of stenosis was between the left common carotid and the left subclavian arteries. The condition was diagnosed during life and proved by postmortem examination. The case reported is of further interest because of the presence of a congenitally bicuspid aortic valve which was the seat of subacute vegetative endocarditis.

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THROMBOANGIITIS OBLITERANS IN A WOMAN*

Report of a Case

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IT IS well known that thromboangiitis obliterans rarely affects women, but no adequate explanation has ever been given. Only about twenty-two satisfactory cases are on record. In Buerger's series[1] of 500 cases there were 2 women; in Koyano's series[2] of 120 there was one; in Horton and Brown's series[3] of 700 there were 10; in Herrell and Allen's series[4] of 350 there was one; and in Silbert's series[5] of 1,200 there were 2. In addition, single cases have been reported by Meleney and Miller,[6] Telford and Stopford,[7] Dürck,[8] Traubaud and Chaty,[9] Traubaud and Mredden,[10] and Van Dellen and Wright.[11]

REPORT OF CASE

S. K., a married Russian Jewish woman, 27 years of age, was admitted to the hospital May 11, 1937, and discharged July 8, 1937. She gave a history of intermittent claudication due to pain in the calf of the right leg of two years' duration. Two weeks before admission severe pain developed in the fifth right toe, which became infected and discolored. During her fourth pregnancy, three years before, she had had some "trouble" with the veins in both legs. The patient had been a cigarette smoker for many years, and in the two years preceding admission had smoked between 40 and 60 cigarettes a day. Once every year, for ten years, she had taken about 2 ounces of the fluidextract of ergot to induce abortion. The last dose was taken four months before admission. She had always noticed numbness and tingling of the extremities soon after taking the drug.

Physical Examination.—There were no abnormalities except in the lower extremities. Both feet were cold, the right more so than the left. Dependent rubor and blanching with elevation were very evident in both legs. No pulse could be felt in either dorsalis pedis or posterior tibial artery. There was a small area of gangrene on the fifth toe of the right foot.

Oscillometric Readings

	Foot	*Ankle*	*Below Knee*	*Mid-Thigh*
Right	0	0	0	1½
Left	0	1	1	1½

The blood pressure was 90/60. Ophthalmoscopic examination showed nothing remarkable.

Laboratory Examination.—The electrocardiogram was normal. Roentgenograms of the feet and legs revealed no evidence of calcification of arteries. The basal

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metabolic rate was -3 per cent. Agglutination tests for the presence of typhoid, paratyphoid, and typhus antibodies were negative. The Kline test was negative. The blood calcium was 9.7 mg. per cent; the nonprotein nitrogen of the blood, 29.8 mg. per cent; the blood cholesterol, 170 mg. per cent; and the plasma protein, 6.73 gm. per cent (albumin 3.85 gm. per cent, globulin 2.9 gm. per cent, albumin-globulin ratio 1.3). The hemoglobin was 85 per cent; the erythrocytes numbered 4,400,000; and there was a slight leucocytosis. Blood volume studies gave the following result:

Hematocrit (packed cells)	43.3	per cent
Plasma volume	2108	c.c.
Total blood volume	3703	c.c.
Blood volume per kilogram	68	c.c. (85 c.c. is normal)

Subsequent Course.—During the first month of her stay in the hospital the patient received 250 c.c. of a 5 per cent salt solution intravenously every forty-eight hours. Thereafter, for one month, she received 3 c.c. of tissue extract (Sharpe and Dohme) intramuscularly every forty-eight hours. When she left the hospital the gangrenous area was healing, but there was still no pulse in the dorsalis pedis artery. Treatment with 5 per cent salt solution was continued in the outpatient department.

Examination Oct. 26, 1937, showed that the gangrenous area had healed, but there was no pulse in the dorsalis pedis or posterior tibial artery, and the right foot was still colder than the left.

Oscillometric Readings

	Foot	*Ankle*	*Below Knee*	*Mid-Thigh*
Right	0	0	0	2
Left	0	1½	1½	3

Except for moderate claudication due to pain in the right calf, she felt perfectly well.

COMMENT

Silbert and his associates,[12, 13, 14] in their study of thromboangiitis obliterans, found that the basal metabolic rate was low, that the blood was concentrated and its volume reduced, and that the amounts of blood proteins, calcium, and cholesterol were increased. In my case none of these abnormalities except reduced blood volume was noted.

It is doubtful if ergot played an etiologic role in this case. The patient had taken only 10 doses in ten years, and there had never been a severe local reaction.

CONCLUSION

The foregoing case is reported because of the rarity of thromboangiitis obliterans in women. The patient was a young Russian Jewess who had abused tobacco, gave a history of intermittent claudication, and had a painful, gangrenous area on one toe. Dependent rubor and pallor with elevation were evident in both legs, both feet were cold, and no pulse could be felt in either dorsalis pedis or posterior tibial artery. There was no evidence of peripheral arteriosclerosis.

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ACUTE ISOLATED MYOCARDITIS

Report of a Case, With a Study of the Development of the Lesion* †

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THE term "acute isolated myocarditis," now used instead of "acute primary myocarditis," should designate a disease in which inflammation of the myocardium is the only important active acute lesion in the body. The disease may be due to actual infection of the myocardium, or, as in experimental animals and very probably in man, to the effect of chemical action alone or chemical and other factors acting simultaneously on the heart. In some cases the etiology remains obscure, hence the term "idiopathic." The disease regularly runs its full course without being recognized, despite the fact that it has been periodically considered and quite well defined in the foreign medical literature during the past thirty-six years. It is only recently that a few reports have appeared in the American literature. Our recent experience with a case prompted us to make a survey of the literature, from which we learned that there is a group of symptoms which seem distinctive. Our survey was extended to include the various chemicals used singly or in combination in the experimental production of acute myocarditis. We wished to know particularly whether experimental myocarditis paralleled acute isolated myocarditis in severity of injury and reaction. Our own case afforded an unusually good opportunity to study the development of the myocardial lesions. By reporting it, and summarizing the important clinical and pathologic characteristics of all the cases in the literature, we hope to facilitate the diagnosis of this elusive disease.

REPORT OF CASE

Clinical Examination.—C. G. (105252), a well-developed and well-preserved colored woman, 48 years of age, entered the Gallinger Hospital, Washington, D. C., Oct. 17, 1933, and died suddenly Oct. 20, 1933. She had suffered since early in the summer of 1933 from what she called a bad chest cold, which was followed by cough and the expectoration of a large amount of frothy sputum. The sputum was twice bloodstained. The patient complained of much weakness and said that she had lost 20 pounds. She thought that she had had fever at times, but her temperature had not been taken. She continued to do her housework until two weeks before her admission to the hospital, when she was forced to go to bed because of extreme weakness, shortness of breath, and fever. The only gastrointestinal findings of note were blood in the feces on two occasions and a filling defect at the pylorus which was thought to be caused by spasm. She had been treated for syphilis, but did not remember when, for how long, or by what means.

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The temperature on admission was 99.6° F., and the blood pressure was 100/79. The gums were puffy and bled easily, the teeth were carious, and there was enlargement of the cervical lymph nodes. A few râles were heard at the apices of both lungs. The heart was normal to physical examination. A definite mass which was thought to pulsate was felt in the midline in the epigastric region; the epigastrium was tender and tense. The liver was palpable.

Clinical Laboratory Examination.—The hemoglobin was 80 per cent. The leucocytes numbered 18,000 per cu. mm., and the differential leucocyte count showed that 50 per cent were lymphocytes, 2 per cent large mononuclear cells, 44 per cent polymorphonuclear cells, and 3 per cent nonfilamented polymorphonuclear cells. The Kahn test was strongly positive.

Clinical Course.—The temperature varied from 99° to 99.6° F. until the day before death, when it rose to 102° F. The pulse rate ranged from 100 to 110, and the respiratory rate from 20 to 28. There were no complaints other than weakness and

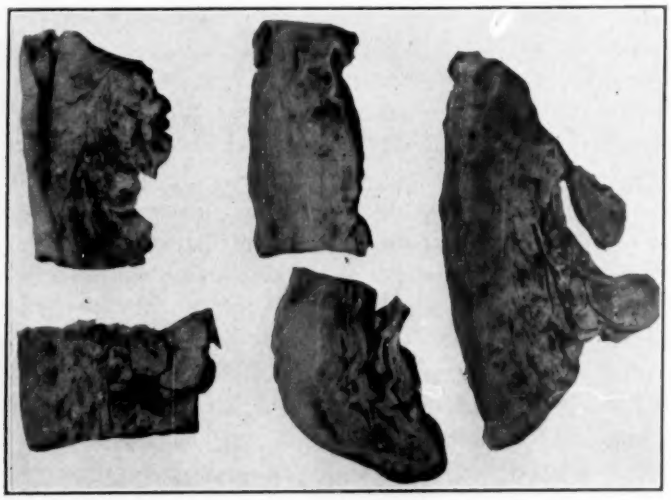

Fig. 1.—Cut sections of the myocardium. The gray appearance and the numerous hemorrhagic foci are striking.

dyspnea. On the evening of October 21, the patient felt very uncomfortable and restless, and ¼ grain of morphine sulfate was administered. One hour later she was found dead in bed.

Post-Mortem Examination.—The body was that of a well-developed and excellently nourished woman. *Rigor mortis* was marked. Cyanosis of the finger tips, lips, and dependent portions of the body was extreme. There was no edema. The teeth were carious and the gums swollen. The layer of fat in the midline over the chest and abdomen was from 1 to 2 cm. thick. The internal genitals were the seat of an old, quiescent inflammatory process. Moderate enlargement of lymph nodes was found over the pericardium, in the region of the thymus gland, and in the neck and abdomen. The nodes at the hilum of the liver were especially enlarged, the largest measuring 2 cm. in diameter. The heart weighed 300 gm. and was normal as far as muscle mass was concerned. There was no dilation. The myocardium was somewhat gray and translucent. There were petechiae beneath the endocardium, including that of the papillary muscles, and the left ventricular surface of the interventricular septum contained large ecchymoses. On section, there were distinct gray areas about 2 mm. in diameter framed by a zone of hyperemia and hemorrhage. These lesions were most conspicuous in the left ventricle and interventricular septum, but were also

present, in descending order of frequency, in the right ventricle, right auricle, and left auricle. The lesions appeared to be contained entirely within the myocardium. The coronary vessels were normal. The pericardium and endocardium were smooth and glossy. The right lung weighed 250 gm., the left 220 gm.; the alveoli contained frothy fluid. The spleen weighed 110 gm.; it was not grossly abnormal. The duodenal mucosa was greatly congested, and the pancreas showed post-mortem digestion. The liver weighed 1,100 gm., and its edges were rounded. The hepatic veins were dilated. The right kidney weighed 125 gm., the left 150 gm.; both appeared normal. There were a few atheromatous plaques in the aorta. The bladder was not inflamed. The thyroid gland was normal in size, and its cut surface appeared normal. The trachea, larynx, and pharynx were removed, and appeared to be normal.

Histologic Examination.—The only important pathologic changes, other than the enlarged lymph nodes, were found in the myocardium, which contained lesions in various stages of development. The most recent lesions consisted of fractured hyalinized muscle fibers which had lost their striations, and in these areas definite hemorrhages were observed. Others which appeared to be further developed revealed, in addition to the muscle injury and hemorrhage, numerous polymorphonuclear leucocytes. Still others contained remnants of hydropic and fatty muscle fibers and many lymphocytes and large mononuclear cells. Many of the latter contained hemosiderin. There were also areas of quite well-developed scar tissue which was arranged in a columnar pattern as if it had replaced individual muscle fibers. A few myocardial giant cells were present in some of these areas. Here and there exudate extended into the interstitial tissue. The coronary vessels appeared normal. The remaining organs showed acute edema and congestion. The enlarged lymph nodes were simply hyperplastic. There was no histologic evidence of syphilis as described by Warthin. There was but slight atheromatous change in the aorta. The thyroid and adrenal glands were normal.

Bacteriologic Examination.—Smears and cultures made from the nose and throat at the time of post-mortem examination showed streptococci, but no organisms or colonies which resembled the *Corynebacterium diphtheriae.* Numerous sections of the myocardium stained by the Warthin-Starry method failed to reveal the *Treponema pallidum,* although organisms in control material were well stained. Bacterial stains also failed to reveal other organisms in the myocardium.

EPICRISIS

We have no reason to suppose that this patient suffered from anything other than myocardial injury after the beginning of her illness early in the summer of 1933. There was no evidence of generalized systemic infection, and therefore, if bacteria are to be held responsible for the myocardial injury, one must fall back on the somewhat doubtful assumption of focal infection. The patient had had leucorrhea, but the cervix did not appear to be particularly abnormal. The swollen gums and carious teeth were possible foci of infection. The outstanding clinical features were weakness, cyanosis, and dyspnea. The patient was well-nourished and appeared to be in good health throughout most of her illness, and there was no hypertrophy or dilation of the heart and no edema of the extremities. A priori, one would expect the lesions of isolated myocarditis to be evenly distributed. In this case they were most numerous in the wall of the left ventricle and the interventricular septum, which fact suggests that the higher left ventricular pressure

Fig. 2. Fig. 3.

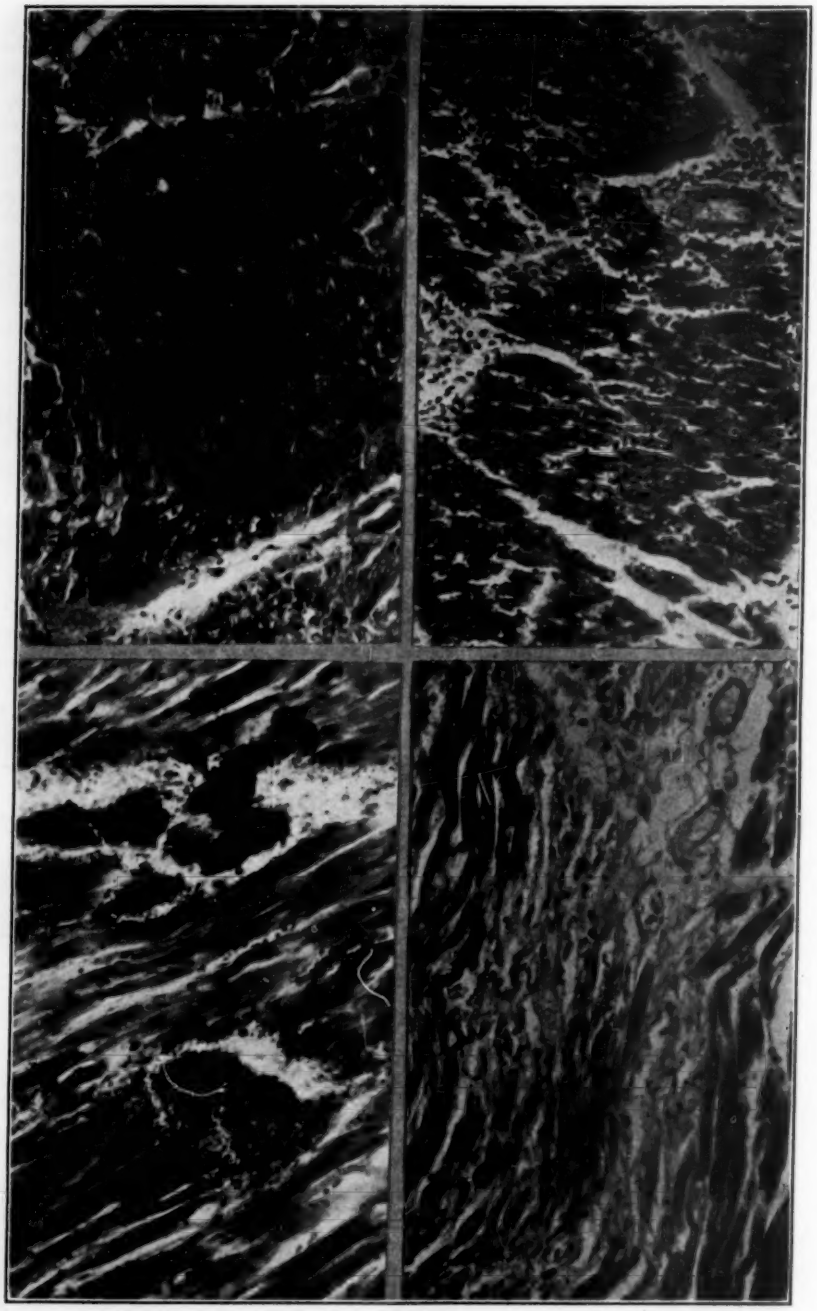

Fig. 4. Fig. 5.

Fig. 2.—Photomicrograph (×205) showing an area of early injury to the myocardial fibers, as indicated by the intense staining reaction and early cellular infiltration.

Fig. 3.—Photomicrograph (×205) showing the diffuse inflammatory cellular infiltration within and between the muscle fibers.

Fig. 4.—Photomicrograph (×250) illustrating the fractured muscle fibers and hemorrhage. Many severely injured unfractured muscle fibers are also seen.

Fig. 5.—Photomicrograph showing the parallel arrangement of scar tissue in which fragments of muscle fibers are enmeshed.

may have been a factor in their distribution. The sequence of events in the development of the lesion appeared to be (1) injury of muscle fibers, (2) fracture of muscle fibers with hemorrhage, (3) leucocytic infiltration, (4) clearing away of fragments of tissue by macrophages, and (5) scarring. This is not unlike Zenker's degeneration of voluntary muscle. The fact that so many of the hyalinized muscle fibers were fractured makes one suspect that the same thing occurs in the milder forms of toxic myocarditis from which patients usually recover. It may be that the loss of these fibers increases the demands on those which survive, with the result that hypertrophy and dilation of the heart eventually occur. Moreover, this may explain the tremendous hypertrophy and dilation in cases in which the coronary arteries are not significantly narrowed and hypertension has not been a factor. Saltykow[10] has also maintained that acute myocarditis leads ultimately to myocardial fibrosis and hypertrophy.

Acute isolated myocarditis was first described by Fiedler,[5] who included in his report only cases in which the myocarditis was the sole lesion. Subsequent contributions have been made by Saltykow,[10] Scott and Saphir,[12] de la Chapelle and Graef,[3] Bailey and Andersen,[1] and others. Warthin[13] described isolated myocarditis due to the *Treponema pallidum* which he interpreted as an acute exacerbation of chronic syphilitic myocarditis similar to the critical reaction observed by Brown and Pearce[2] in their experimental animals.

Not all authors have excluded, as Fiedler[5] did, cases in which myocarditis was not the sole lesion. Many were complicated by systemic infection or by other kinds of heart disease. Those in which infection was present might not differ greatly from cases of myocarditis following diphtheria, scarlet fever, severe burns, or influenza. At best, it would be difficult to distinguish the symptoms referable to acute myocarditis from those which were caused by the accompanying condition.

The important clinical and pathologic features of *uncomplicated* acute isolated myocarditis, as recorded in the literature, are summarized in Tables I and II. The occupations are not tabulated, but sixteen different ones were represented. The close clinical similarity between this disease and coronary occlusion is striking. However, ten of the patients were rather young for coronary occlusion, and the extremely severe precordial pain which appears suddenly and tends to radiate is not characteristic of acute isolated myocarditis. Rapidly developing myocarditis is more likely to be signalized by comparatively mild precordial distress and a chill. The patient is restless, apprehensive, short of breath, cyanotic, and may complain of weakness, palpitation, and irregularity of the heart. By the time these symptoms have appeared the heart is usually enlarged, indicating that the pathologic process begins long before the symptoms. Therefore, if we are to discover the etiologic agent, we must

not neglect to question the patient carefully about the events, however trivial, of the months immediately preceding the first unequivocal symptom.

TABLE I

THE IMPORTANT CLINICAL FEATURES OF ACUTE ISOLATED MYOCARDITIS

CASE NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
AGE	53	42	45	25	45	44	57	22	53	35	22	42	24	21	21	39	26	48
DURATION (DAYS)	1	2	1	3	3	1	1	14	90	14	8	7	6	18	8	14	90	150
SYPHILIS	+	+	0				+								0			0
WASSERMANN									0	0				0			0	+
RESTLESSNESS	+								+		+	+	+	+		+	+	+
DYSPNEA	+		+	+	+	+	+		+	+	+	+	+	+	+	+	+	+
CYANOSIS	+	+	+	+		+				+	+	+	+	+	+	+	+	+
PRECORDIAL PAIN	+	+			+	+	+		+	+	+	+	+		+	+	+	
WEAKNESS	+	+				+	+			+	+	+	+	+	+	+	+	+
FROTHY SPUTUM				+								+			+			+
ABDOMINAL PAIN	+												+			+		
ARM PAIN	+					+	+									+		
ENLARGED HEART									+	+		+	+		+		+	
FEVER									+	0	0	+	+	+	0		+	+
ARRHYTHMIA									+	+	+	+	+		+		+	
MODE OF ONSET	S	S	S	S	S	S	S				SC	G	SC	G	G	G	G	G
MODE OF DEATH	S	S	S	S	S	S	S		S	S			S	S	G	S	G	S
PALPITATION					+				+	+	+						+	
EDEMA											0	0	0	0	+		0	0
LEUCOCYTOSIS														+	+			+
HEART RATE											152	148	38	140	92		140	110
SWEATING											+		+		0	+		0

LEGEND – + = PRESENT 0 = ABSENT S = SUDDEN G = GRADUAL
C = CHILL BLANK SPACE = NO STATEMENT

TABLE II

THE IMPORTANT PATHOLOGIC FEATURES OF ACUTE ISOLATED MYOCARDITIS

CASE NO.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
LYMPHOCYTES	+	+	+	+	+	+	+	+	+		+	+	+	+	+	+	+	+
NEUTROPHILES	+	+	+	+	+	+	+	+	+	+	+	+	+			+	+	+
PLASMA CELLS	+	+	+	+	+	+		+	+						0	+	+	+
MONOCYTES							+	+	+					+	+	+		+
EOSINOPHILES								+	+	+	+	+	+			+	+	+
GIANT CELLS								+							0		+	+
DILATION	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0
HYPERTROPHY		+		+	+	+	+	+	+	+	+	+	+	+	+	+	+	0
MYOCARDIAL INJURY	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	0	+	+
PERICARDITIS			+					0		0	0				0	0	0	0
MURAL THROMBUS			+	+				+	+	+		0		+	+	+	0	0
CORONARY OCCLUSION								0	0	0	0	0	0		0			0
MYOCARDIAL HEMORRHAGE								+		+	+	+	+	+			+	+
MYOCARDIAL SCARRING	+	+	+	+			+									+	+	+
GENERAL EDEMA									+	+	0	0	0	+	+		0	0
SPIROCHETES	+	+	+	+	+	+	+								0		0	0
OTHER ORGANISMS										+	0	0	0	0	0	0	0	0

LEGEND – + = PRESENT 0 = ABSENT BLANK SPACE = NO STATEMENT

Except for the cases reported by Warthin, in which the *Treponema pallidum* was regularly demonstrated, investigators have been uniformly

unsuccessful in their search for bacteria in the myocardial lesions. Rindfleisch[9] isolated an organism from the myocardium which he called *Staphylococcus citreous,* but it did not cause abscesses, and he was unable to demonstrate its presence histologically; its etiologic relationship to the lesions in the myocardium must be regarded as doubtful. Most authors are of the opinion that the myocardial injury is due to bacterial toxins circulating in the blood. The pathologic changes which have been described do not enable one to distinguish between the cases in which the Treponema was present in the tissue and those in which no organisms were found. The hypertrophy and dilation of the heart, the scarring in some of the lesions, and the myocardial giant cells indicative of a reparative process are the earmarks of a steadily progressive and insidious disease which leads to sudden and unexpected death.

The histologic examination in our case was very enlightening. The fact that lesions were observed in all stages of development betrayed the progressive nature of the disease. The myocardial injury was diffuse, but the development of focal defects seemed to be dependent upon fracture of the hyalinized muscle fibers, followed by hemorrhage, exudation, and the formation of scar tissue in columns which exactly replaced the original muscle fibers. The free ends of the affected muscle fibers were thus bound together. These observations indicate that the process is not primarily an interstitial one, as many previous authors have supposed.

Many chemical agents have been employed, alone or in combination, to produce acute experimental myocarditis. The best results have been obtained by combining sparteine with adrenalin, or chloroform with thyroxin or desiccated thyroid substance, but the lesions produced are not comparable in severity with those of acute isolated myocarditis. The fact that in acute infectious diseases the heart usually escapes and that acute isolated myocarditis is rare would indicate that more than one factor is concerned in acute myocarditis, and that one of these factors must be of bacterial origin (e.g., the diphtheria or streptococcus toxin).

In the final analysis, acute isolated myocarditis differs etiologically from the acute toxic myocarditis which is caused by infectious diseases only in that the origin of the infectious agent is obscure. We have already learned to recognize the cardiac complications of the infectious diseases and should experience still less difficulty with the diagnosis of acute isolated myocarditis, for the latter is not accompanied by the misleading protean manifestations of the generalized infectious process.

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Department of Reviews and Abstracts

Selected Abstracts

Freeman, Norman E., and Zeller, J. Wallace: The Effect of Temperature on the Volume Flow of Blood Through the Sympathectomized Paw of the Dog With Observations on the Oxygen Content and Capacity, Carbon-Dioxide Content, and PH of the Arterial and Venous Blood. Am. J. Physiol. **120**: 475, 1937.

Experiments have previously been performed in humans, studying the effect of temperature on the rate of blood flow in the sympathectomized hand. The results of these studies suggested a dual control of the circulation, indicating that the flow of blood is modified by the vasomotor nerves to meet the requirements for thermoregulation of the body as a whole. After removal of the vasomotor control, the circulation seems to be dependent upon the metabolic requirements of the tissues. The results of the experiments as carried out in man were somewhat variable; this was considered to be due to reflex secretion of adrenine induced by unavoidable emotional disturbances. In order to eliminate the adrenal factor, similar experiments have been carried out on dogs in which one adrenal gland had been removed and the other had been denervated. The oxygen content, carbon-dioxide content, and pH of the arterial and venous blood were studied in three unanesthetized, trained dogs in which one adrenal had been removed and the other denervated. The volume flow of blood in the sympathectomized paw of these animals was measured by plethysmographic determinations. It was found that the oxygen and carbon-dioxide contents and pH difference in the arterial and venous blood were constant in a single experiment over wide ranges of blood flow and metabolism. The volume flow of blood through the paw varied directly with the temperature of the bath in which the paw was immersed. These findings are consistent with the hypothesis that the circulation through regions deprived of vasomotor control is controlled by the metabolic needs of the tissues.

HINES.

László, T.: Physiology of Adrenal Cortical Hormones. Cardiologia **1**: 219, 1937.

Simultaneous removal of both adrenals has no effect on the specific conducting system of the heart in dogs killed shortly before the time of expected death. Cortical extracts used in these studies, according to the author, were considered unsatisfactory, and the results may have been due to impurities rather than to the hormone itself.

KATZ.

Puddu, V.: Concerning the Action of Cardiac Nerves. Arch. f. d. ges. Physiol. **238**: 467, 1937.

Observations on the dog show that the sympathetics change the electrocardiographic contour. Unipolar leads from the ventricles indicate that the right and left nerves have action on different regions. Following complete heart block in

the dog, it was found that vagus stimulation slowed the idioventricular rhythm. This is attributed to transmission of cholinergic material liberated in the auricle.

KATZ.

Rühl, A., and Thaddea, S.: Dynamics and Metabolism of Heart Poisoned With Monoiodoacetic Acid. Ztschr. f. Kreislaufforsch. 30: 26, 1938.

Monoiodoacetic acid in doses of 250-500 mg. caused pulmonary edema in the heart-lung preparation of the dog, and later damage to the heart. The coronary vessels showed a marked dilatation. The pulmonary edema can be delayed by prophylactic doses of strophanthin. Lactic acid consumption of the heart is increased by monoiodoacetic acid, and the glycogen content of the heart muscle is increased. The respiratory quotient is usually decreased. Muscular hemorrhages occurred and these probably explain the electrocardiographic changes.

KATZ.

Schneider, Edward C., and Collins, Raymond: Venous Pressure Responses to Exercise. Am. J. Physiol. 121: 574, 1938.

A comparison of the Eyster, Hooker, and White methods of determining venous pressure shows that each gives the same account of the changes that result from physical exertion.

The venous pressure rises and then remains up during work on the bicycle ergometer. In some individuals the pressure begins to rise almost at once, reaches a maximum within two to four minutes, and then maintains a fairly steady state. In others after some delay a slow rise begins, reaches a maximum within ten to twelve minutes, and then remains fairly constant until work is terminated.

When the load of work is too heavy, the venous pressure rises steadily until fatigue ensues.

There is a rough linear relationship between venous pressure and load. This may be obscured by the deep breathing of exertion, since during expiration the venous pressure may be as much as 2 cm. H_2O higher than during inspiration.

After physical exertion the venous pressure ordinarily slowly returns to normal. This may be accomplished within a few minutes, but after heavy work often requires as much as twenty-two to twenty-seven minutes.

AUTHOR.

Gibson, John G., and Evelyn, Kenneth A.: Clinical Studies of the Blood Volume. J. Clin. Investigation 17: 153, 1938.

A photoelectric method of determining the dye concentration of serum samples in the plasma volume method of Gibson and Evans is described.

Comparison of this method with that employing the spectrophotometer proves it to be accurate within a range of ±2.5 per cent in a series of plasma volume determinations.

For purposes of clinical research the simplified technique is as reliable as the spectrophotometric method and possesses the added advantages of greater simplicity, economy, speed, and freedom from subjective errors.

AUTHOR.

Pezzi, C., and Agostoni, G.: Concerning Stenosis of the Aorta in the Region Between the Arch and Descending Portion. Cardiologia 1: 125, 1937.

In the authors' review of this subject, the greater frequency of that form of stenosis occurring where the ductus Botalli is situated, and the rarity of clinically

visible arterial collaterals in the thoracic region are pointed out. The x-ray picture is typical of stenosis of the aorta. It shows the enlarged left ventricle, the usually dilated ascending aorta, and the characteristic notching of the posterior lower margins of the ribs.

KATZ.

Rothberger, C. J.: Concerning the Normal and Pathological Physiology of the Specific Conducting Tissue of the Heart. Cardiologia 1: 234, 1937.

An excellent review is presented of the subject with which the author has long been identified. The article must be read for the details. Among the facts brought forth, the following may be mentioned: (1) the refractory phase of Purkinje fibers is longer than that of ordinary ventricular muscle; (2) as the strength of stimulus to the Purkinje fibers was decreased, failure to respond to some of the impulses was found to occur before the stage was reached where all became ineffective; (3) the duration of the electrogram of the Purkinje fibers is longer than its refractory phase and contraction, (4) veratrin in small doses leads to runs of beats with pauses between them and (5) Purkinje fibers are not as susceptible to low oxygen content as auricular strips.

KATZ.

Takino, M., and Watanabe, S.: The Significance of the Ligamentum Arteriosum of the Ductus Botalli and Its Junction with the Pulmonary Artery as a Blood Pressure Regulator in Various Animals. Arch. f. Kreislaufforsch. 2: 18, 1937.

In the embryo and young animal (rabbit, dog, cat, and fetus of man) this region contains end organs which set up reflexes to help adjust the circulation. As the ductus degenerates into a ligament, the end organs move from the aortic attachment to the pulmonary artery and still function.

KATZ.

Schellong, F., Schwingel, E., and Germann, H.: Vector Diagraphy and the Normal Vectordiagram. Arch. f. Kreislaufforsch. 2: 1, 1937.

This is a description of the method previously reported by the authors of using thoracic leads with stereoscopic orientation. In 100 normal persons the spatial contour of the vector diagram was determined during the inscription of the QRS complex and also during that of the T-wave. The QRS vector has an elliptical form which may be interrupted by flat indentations. It starts from zero and moves forward to the left and down and then backward to the right and then up. At its start it first moves up and at its end moves down. The T-wave forms a smaller similar elliptoid. The angle between the end of the QRS and T elliptoids is determined and was found in all but 4 cases to be less than 45 degrees. This spatial vector derived from thoracic leads is more satisfactory than the one derived from leads from the extremities.

KATZ.

Spang, K., and Korth, C.: Alternans of the Ventricular Complex of the Human Electrocardiogram. Arch. f. Kreislaufforsch. 2: 47, 1937.

The literature is reviewed by the authors and ten cases are reported. Alternans of groups of beats as contrasted with alternans between beats is described. One cannot separate electrical from mechanical alternans.

KATZ.

Hadorn, W.: Observations of the Heart in Hypoglycemic Shock (in Relation to the Electrocardiographic Changes in Insulin Treatment of Schizophrenia With Notes on the Effect of Cardiazol on the Electrocardiogram in the Same Condition). Arch. f. Kreislaufforsch. 2: 70, 1937.

This is a presentation of monographic proportions which covers over 80 pages and contains the author's extensive studies correlating work on animals and patients.

Insulin shock in schizophrenic and in normal subjects causes, in many persons, tachycardia and a rise in blood pressure with increased pulse pressure and venous pressure. Angina pectoris may also occur in diabetics with coronary sclerosis, but similar pain may be found in schizophrenics without heart disease. These changes are attributed in part to a liberation of adrenalin. It is concluded that insulin is to be used cautiously in coronary sclerosis.

In the electrocardiogram insulin causes increased amplitude of P and QRS, prolongation of QRS and P-R, coronary nodal rhythm, extrasystoles of auricular and ventricular origin, depression of S-T, prolongation of electrical systole, and flattening and inversion of T. These electrocardiographic changes indicate again the hazard of insulin usage in coronary disease. Cardiazol (tetrazol) causes much less change in the electrocardiogram than does insulin. There is, however, a tendency toward auricular extrasystoles and auricular fibrillation.

KATZ.

Albers, D., and Thaddea, S.: Electrocardiographic Changes in Experimental and Clinical Adrenal Insufficiency. Ztschr. f. Kreislaufforsch. 29: 825, 1937.

Adrenal insufficiency causes decreased amplitude of deflections, depression of S-T, and inversion of T. The deviations tend to return toward normal when the cortical hormone is supplied. The damage to the heart muscle was demonstrated histologically, but not in all cases.

KATZ.

Bellet, Samuel, and McMillan, Thomas M.: Electrocardiographihc Patterns in Acute Pericarditis: Evolution, Causes and Diagnostic Significance of Patterns in Limb and Chest Leads; A Study of Fifty-Seven Cases. Arch. Int. Med. 61: 381, 1938.

The electrocardiographic findings in fifty-seven cases of acute pericarditis of different etiologic types are presented and discussed.

On the basis of these observations it is concluded that in a large majority of cases (80 per cent in this series) electrocardiographic changes are associated with pericarditis. In twenty-one cases (more than 37 per cent) the alteration in the RST segment conformed to a pattern which we regard as fairly characteristic, namely, elevation of the RST segment in the three limb leads, depression of the interval in Leads IV and V and elevation of the interval in Lead VI, with preservation of the initial downward deflection. In the remainder the inversion of the T-wave and minor changes in the RST segment, which are considered important, were noted. In the main, the deviation in the RST segment was observed in association with the more virulent forms of pericarditis, e. g., pneumococcic, uremic, and rheumatic; the alteration in the T-wave was the outstanding change present in cases of tuberculous pericarditis.

The deviation in the RST segment and the change in the T-wave are transient; for this reason it is important to obtain electrocardiographic records at frequent intervals.

The use of precordial leads as an important aid in the diagnosis is herein recorded; additional information was sometimes obtained by placing the anterior electrode over the area of friction.

The basing of a differential diagnosis on the electrocardiographic findings in cases of pericarditis and coronary occlusion is discussed.

Histologic studies of the cardiac muscle were made in nineteen of the cases of our series. From these observations, together with other factors mentioned, it is concluded that invasion of the subpericardial portion of the myocardium by pericarditis is chiefly responsible for the deviation observed in the RST segment.

Frequently, in spite of the presence of frank pericarditis, no electrocardiagraphic changes are observed. This is probably due to the absence of myocardial involvement or to the presence of an extremely slight grade of involvement.

AUTHOR.

Weicker, B., and Kessler, M.: Malaria and the Electrocardiogram. Ztschr. f. Kreislaufforsch. 30: 9, 1938.

Curves were taken on 25 patients with neurosyphilis during malarial therapy. In several instances changes were found indicative of coronary insufficiency. The majority, however, showed only minor changes, During treatment, the electrocardiogram may be a valuable adjunct in bringing to light latent myocardial damage in these patients.

KATZ.

Travell, Janet, Gold, Harry, and Modell, Walter: Effect of Experimental Cardiac Infarction on Response to Digitalis. Arch. Int. Med. 61: 184, 1938.

In the present study of fifty cats the effect of digitalis on the control animal is compared with that on the animal three weeks after experimental ligation of a coronary vessel with respect to the following points: the fatal dose, the dose necessary to produce a ventricular ectopic rhythm, the effect on the blood pressure, the changes in the R-T segment of the electrocardiogram, and the degree of healing of the infarct.

Previous studies have shown that within the first twenty-four hours after the experimental production of cardiac infarction the tolerance to digitalis is the same as that of the normal animal (cat and dog). In the presence of a partially healed infarct the cat (as well as the dog) is more susceptible to digitalis than the normal animal, requiring only about three-fourths as much digitalis as the normal animal to cause (a) a ventricular ectopic rhythm and (b) death. The larger the infarct, the more susceptible the animal; but many exceptions to this rule were observed, and some of the most susceptible animals had the smallest infarcts.

Treatment with aminophylline appeared to exert no effect on the tolerance to digitalis in cardiac infarction.

There is some indication that digitalis may cause displacement of the R-T segment in the electrocardiogram more readily in animals with cardiac infarction than in the normal animal.

Differences in tolerance may involve equally the fatal dose and that required to cause a ventricular ectopic rhythm, but the range of change tends to be greater for the former than for the latter. This appears to be true of differences in tolerance among apparently normal animals, as well as among those with cardiac infarction.

The facts indicate that increased susceptibility to digitalis in cardiac infarction may be due to a change in the properties not of the whole heart but of an area with impaired circulation within the zone of the infarct, from which abnormal impulses arise as the result of the administration of digitalis and precipitate ventricular tachycardia and fibrillation.

AUTHOR.

Binger, M. W., and Craig, W. McK.: Atypical Case of Hypertension With a Tumor of the Adrenal Gland. Proc. Staff Meet. Mayo Clin. 13: 17, 1938.

A case of essential hypertension is reported in which an adrenal tumor was found at the time of surgery carried out for relief of the hypertension by a resection of the splanchnic nerves. The patient seemed to have a typical case of essential hypertension. However, she had an extreme intolerance to heat and a basal metabolic rate of +61 per cent which could not be explained, as there was no evidence of hyperthyroidism. Following the first-stage operation for splanchnic resection, there was nothing unusual about the postoperative course. However, following the second stage of the operation performed twelve days after the first operation, the blood pressure rose to a very high level and remained so for a period of ten days. It was postulated that this unusual course of events might be due to some change in the right adrenal gland, and the patient was returned to the operating room and the old incision reopened. Immediately above the kidney a large tumor, measuring 6 by 3.5 cm., was found which proved microscopically to be a sympathicoblastoma. Following the removal of this tumor, the blood pressure returned to a low level, and it remained low up to the time of her dismissal. It was thought that the tumor had been activated by the manipulation incidental to the operation and that this was the cause of the excessive blood pressure reaction following the operation, although not necessarily the cause of the persistent hypertension which had been present previous to the operation.

HINES.

Burwell, C. Sidney: A Comparison of the Pressures in Arm Veins and Femoral Veins With Special Reference to Changes During Pregnancy. Ann. Int Med. 11: 1305, 1938.

The arm and leg venous pressures were studied in a group of nonpregnant persons including normal persons and those with conditions already known to affect local or general pressure and in a group of pregnant women and pregnant dogs. The direct method of measuring venous pressure described by Moritz and von Tabora was used in this study. The test was performed with the patient in the supine position in bed and with the zero of the manometer set at a level 5 cm. dorsal to the fifth dorsal cartilage. In individuals without heart disease or local obstruction, the venous pressure is nearly identical in the arm and leg under the conditions of this experiment. In the patients with congestive heart failure, the pressures are almost identical in arm and leg unless there is considerable ascites, in which case the leg pressure may be higher than the arm pressure. In pregnant women by the fourth month of pregnancy an increase takes place in the venous pressure in the leg which persists and even may increase throughout pregnancy. It was concluded that this increase was not due to increase in intraabdominal pressure but due to the pressure of the gravid uterus because when a pregnant dog's abdomen was opened the femoral venous pressure did not change. From these studies, it was concluded that venous collaterals developed when there is a higher degree of venous pressure in one area of periphery than in another. The higher pressures which were found in the femoral veins of pregnant women is thought to be due to the inflow of a large amount of blood through the placenta and obstruction of the outflow by the gravid uterus. A comparison of venous pressure in the different parts of the body may be helpful in the understanding and description of disease and may on occasion even be applied to diagnosis.

HINES.

Herrell, W. E.: Idiosyncrasy to Tobacco: Report of Case. Proc. Staff Meet., Mayo Clin. 13: 1, 1938.

A case is reported of a patient with hypertension in whom the smoking of tobacco produced marked elevation of the blood pressure. A rise in blood pressure as high as 60 mm. of mercury systolic and 50 mm. of mercury diastolic would occur after smoking one or two cigarettes. With abstinence from smoking, the blood pressure which had previously been elevated remained at a normal level, and his symptoms were much improved. The rise in the blood pressure after smoking a cigarette was almost identical with the rise produced by the cold pressor test. It was assumed that this patient would give an exaggerated vasoconstrictor response to many different stimuli and that tobacco particularly would produce a marked vasoconstrictor response with a resulting marked elevation of the blood pressure. Further studies regarding the effect of tobacco on the blood pressure should be carried out. It seems to be wise to advise patients who have hypertension to smoke lightly or not at all if tests show that their blood pressure is influenced by the use of tobacco.

HINES.

Goodman, Charles: Thrombo-Angiitis Obliterans and Typhus (Evidence of Etiologic Relationship). Arch. Surg. 35: 1126, 1937.

Success in the treatment of disease, with few exceptions, has not been obtained until the causative factor has been described. In this respect, thromboangiitis obliterans is typical. Many etiologic agents have been considered as the cause of thromboangiitis obliterans, but in no case has there been definite proof that the suspected agent was the real cause of the disease. An etiologic relationship between typhus fever and thromboangiitis obliterans has been suspected for many years. A cutaneous test has been devised which gives a positive reaction over a long period of time in patients who have had typhus. This test is uniformly negative in normal persons and in a group of patients with arteriosclerosis and diabetes. It is almost uniformly positive in a group of 94 adults with thromboangiitis obliterans. These findings are highly suggestive of an etiologic relationship between typhus and thromboangiitis and open the way for further research along this line.

HINES.

Tartakoff, Joseph, and Hazard, J. Beach: Thromboangiitis Obliterans of the Spermatic Cord. New England J. Med. 218: 173, 1938.

A Russian Jew, aged 28 years, presented symptoms of a dragging sensation in the left groin and the left half of the scrotum, of less than four weeks' duration. There were no other symptoms, and no evidence by physical examination of vascular disease in the extremities. There was moderate tenderness of the left spermatic cord, and a palpable mass the size of a cherry in the cord about 1 cm. above the epididymis. The mass was removed surgically. Microscopic examination revealed changes characteristic of thromboangiitis obliterans, with no tubercle-like lesions. The veins, 0.3 to 1.3 mm. in diameter, were occluded by partly organized and partly canalized thrombi. The smaller vessels, including the arterioles, presented patent lumens and normal lining surfaces and vessel walls. Cellular changes consistent with the diagnosis of thromboangiitis obliterans were found. A diagnosis of nonspecific thrombosis of the spermatic venous plexus was considered untenable because a more extensive lesion would be expected than the one found.

MONTGOMERY.

Anthony, A. J., and Loos, W.: The Distensibility of the Blood Vessels of the Human Extremities. I. Ztschr. f. Kreislaufforsch. 30: 1, 1938.

The authors determined the pulse wave velocity of the blood vessels of extremities in normal persons at various internal pressures. They used a large pressure cuff to decrease the effective internal pressure in the vessels. This led regularly to a decrease in pulse wave velocity. The correlation curve between pulse wave velocity and internal arterial pressure characterizes the properties of the vessel wall.

KATZ.

Lent, W.: The Distensibility of Vessels of the Human Extremities. II. Ztschr. f. Kreislaufforsch. 30: 55, 1938.

When pulse wave velocity is correlated with systolic pressure, the curve is found to be shifted to the right in hypertensive and elderly patients, as compared with the normal; but when the correlation is made with diastolic pressure, no difference in the curves of the abnormals and normals is found.

It is shown that the pulse pressure can be computed from the curve relating pulse wave velocity to the systolic pressure.

KATZ.

Kountz, William B., and Smith, John R.: The Flow of Blood in the Coronary Artery in Pathological Hearts. J. Clin. Investigation 17: 147, 1938.

In hearts of patients who have died of heart failure, the coronary blood flow is diminished either absolutely, as in diseases of the coronary arteries and in dilatation of the heart, or relatively, as in hypertrophy.

Under the conditions of these experiments, it appears that any rate of flow less than 0.75 per gram of heart muscle per minute endangers the function of the heart.

Either hypertrophy or dilatation reduces the coronary flow per gram of heart muscle. In hypertrophy this may be accounted for by increase in muscle mass. In dilatation, lengthening and stretching of coronary vessels may be the chief factor.

In dilated hearts the coronary flow is increased during systole and diminished during diastole; a result which is exactly opposite to that found in hearts of normal diastolic volume.

In the dilated heart drugs which tend to decrease the diastolic volume increase the coronary flow, while those which augment diastolic volume diminish the flow. This action also is directly opposite to the phenomena observed in normal, undilated hearts. It suggests that the physical state of the heart, and particularly the degree of dilatation, must be considered in the selection of drugs for the treatment of cardiac disease.

AUTHOR.

Aschoff, L.: Normal and Pathologic Anatomy of Senility. 3. The Circulatory System in Senility. Med. Klin. 33: 353, 1937.

The following changes in senility were observed: (1) decreased heart weight (but in the presence of atherosclerosis and hypertension cardiac hypertrophy was found), (2) valve deformities on the left side, and (3) fatty infiltration of the pericardium. The capillaries were practically unchanged in number.

KATZ.

Albers, D.: Viscosity of Blood in Cardiac Insufficiency. Ztschr. f. Kreislaufforsch. 29: 915, 1937.

Blood viscosity is increased in heart failure. This occurs also in the presence of anemia when the effect of the anemia itself on the viscosity is discounted. The only exception is in thyrotoxicosis. As the patient improves, viscosity goes back toward normal. There is no parallelism between viscosity and blood pressure. Diuretics and venesection and raw food lower blood viscosity.

KATZ.

Kramer, David W.: Periodic or Intermittent Venous Compression in the Treatment of Peripheral Vascular Disease. M. Rec. 147: 99, 1938.

The method is that recently revived by W. S. Collens and N. D. Wilensky. It consists of intermittent, automatic compression of a thigh at a pressure of 30 to 80. mm. Hg.

Thirty patients with peripheral vascular disease were treated for a total of four hundred hours. Twelve had diabetes; seven, Buerger's disease; five, arteriosclerosis; and four, phlebitis.

Twenty of the patients were benefited; five were slightly or temporarily improved; five were not benefited. Cramps and fatigue were relieved; pain did not respond so satisfactorily. An occasional skin temperature reading showed a rise in skin surface temperature averaging 1 to 3° C. in most of the patients tested. An increase in oscillometric readings was noticed immediately after the treatment, and at the termination of treatments, in those tested. The author thinks that intermittent venous occlusion is a desirable addition to the more recent methods of treatment of vascular diseases but considers the negative and positive pressure apparatus as the outstanding contribution.

MONTGOMERY.

Gold, Harry, Otto, Harold, Kwit, Nathaniel T., and Satchwell, Harry: Does Digitalis Influence the Course of Cardiac Pain? A Study of 120 Selected Cases of Angina Pectoris. J. A. M. A. 110: 859, 1938.

The effect of digitalis medication on cardiac pain was investigated in a series of 120 patients with angina pectoris.

The following criteria were used for the selection of these patients: evidence of organic heart disease, absence of signs of congestion, cardiac pain on effort, doing little or no physical work, and faithful cooperation.

The effect studied was the influence on the severity and frequency of attacks of pain and on the capacity for effort without pain. The data were secured in accordance with a plan designed to reduce to a minimum common sources of error and in a manner relatively free from bias by the use of the "blind test."

In all, 243 courses of treatment with fairly large daily doses of digitalis (from 0.2 to 0.6 gm.) were given, each lasting an average of eleven weeks and being alternated with a course of a placebo of lactose or some other agent.

The course of the pain was charted, the habitual status as well as graded departures from it being represented in every case. The causal relation was established by a method relatively free from personal judgments; namely, by comparing sections of the chart representing, respectively, placebo and digitalis periods.

The results show that nearly one-half of all the patients reported a departure from their habitual status on their return visit after the first course of treatment

with digitalis; in about 15 per cent the pain was increased and in about 30 per cent it was diminished. Results bearing a strong similarity to these were obtained, however, during the use of a placebo.

In most cases the change in pain failed to persist when administration of the drug was continued or failed to reappear during repeated courses of digitalis.

In the remaining cases in which the change recurred when the course of digitalis was repeated, it was possible to digitalize fully without any apparent effect on pain by altering the form, color, or flavor of the preparation of digitalis.

It is concluded from these facts that in cases of angina pectoris without congestion the likelihood is negligible that the use of digitalis will, by a direct action on the circulation, increase or diminish cardiac pain.

In view of the fact that the patients of this series were presumably unusually susceptible to cardiac ischemia, the results indicate further that digitalis even in large doses rarely, if ever, produces effective constriction of the coronary arteries in man.

AUTHOR.

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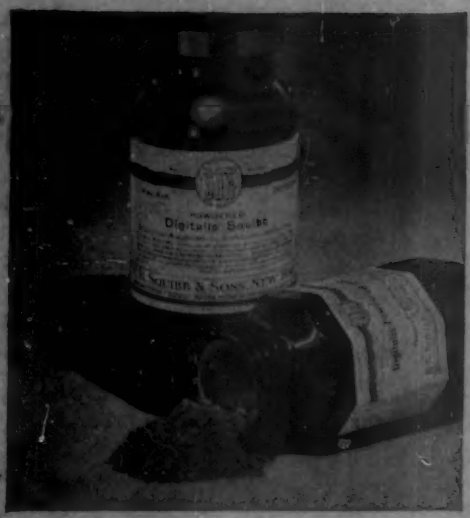

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